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FILE 'HOME' ENTERED AT 12:12:49 ON 20 SEP 2008

=>
=> FIL REGISTRY
COST IN U.S. DOLLARS   SINCE FILE   TOTAL
                                                         ENTRY   SESSION
FULL ESTIMATED COST   0.21   0.21

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STRUCTURE FILE UPDATES: 19 SEP 2008 HIGHEST RN 1050750-61-2
DICTIONARY FILE UPDATES: 19 SEP 2008 HIGHEST RN 1050750-61-2

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predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

http://www.cas.org/support/stngen/stndoc/properties.html

=> s triclosan
L1   5 TRICLOSAN

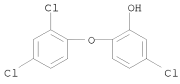
=> d l1 1-5

L1   ANSWER 1 OF 5 REGISTRY COPYRIGHT 2008 ACS on STN
RN   756493-59-1 REGISTRY
ED   Entered STN: 04 Oct 2004
CN   Phenol, 5-chloro-2-(2,4-dichlorophenoxy)-, mixt. with ethanol (9CI) (CA
     INDEX NAME)
OTHER NAMES:
CN   Ethanol-triclosan mixt.
MF   C12 H7 Cl3 O2 . C2 H6 O
CI   MXS
SR   CA
LC   STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

     CM   1

     CRN 3380-34-5
     CMF C12 H7 Cl3 O2

09763499



CM 2

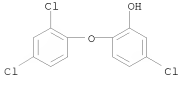
CRN 64-17-5
CMF C2 H6 O

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2008 ACS on STN
RN 756493-58-0 REGISTRY
ED Entered STN: 04 Oct 2004
CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)-, mixt. with 2-propanol (9CI)
(CA INDEX NAME)
OTHER NAMES:
CN Isopropanol-triclosan mixt.
MF C12 H7 Cl3 O2 . C3 H8 O
CI MXS
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

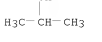
CM 1

CRN 3380-34-5
CMF C12 H7 Cl3 O2



CM 2

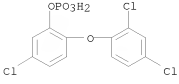
CRN 67-63-0
CMF C3 H8 O



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

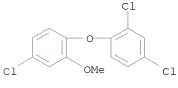
L1 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2008 ACS on STN
RN 67651-57-4 REGISTRY
ED Entered STN: 16 Nov 1984
CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)-, 1-(dihydrogen phosphate) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)-, dihydrogen phosphate (9CI)
OTHER NAMES:
CN Triclosan monophosphate
DR 163886-25-7
MF C12 H8 Cl3 O5 P
LC STN Files: BIOSIS, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

22 REFERENCES IN FILE CA (1907 TO DATE)
22 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L1 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2008 ACS on STN
RN 4640-01-1 REGISTRY
ED Entered STN: 16 Nov 1984
CN Benzene, 4-chloro-1-(2,4-dichlorophenoxy)-2-methoxy- (CA INDEX NAME)
OTHER NAMES:
CN 2,4,4'-Trichloro-2'-methoxydiphenyl ether
CN 5-Chloro-2-(2,4-dichlorophenoxy)anisole
CN Methyl triclosan
CN Triclosan methyl
MF C13 H9 Cl3 O2
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CSNB, TOXCENTER, USPATFULL, USPATOLD
(*File contains numerically searchable property data)

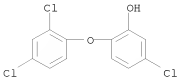


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

37 REFERENCES IN FILE CA (1907 TO DATE)
38 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2008 ACS on STN
RN 3380-34-5 REGISTRY
ED Entered STN: 16 Nov 1984
CN Phenol, 5-chloro-2-(2,4-dichlorophenoxy)- (CA INDEX NAME)
OTHER NAMES:
CN 2',4',4-Trichloro-2-hydroxydiphenyl ether
CN 2',4,4'-Trichloro-2-hydroxydiphenyl ether
CN 2'-Hydroxy-2,4,4'-trichlorodiphenyl ether
CN 2,2'-Oxybis(1',5'-dichlorophenyl-5-chlorophenol)
CN 2,4,4'-Trichloro-2'-hydroxydiphenyl ether
CN 2-Hydroxy-2',4,4'-trichlorodiphenyl ether
CN 3-Chloro-6-(2,4-dichlorophenoxy)phenol
CN 4-Chloro-2-hydroxyphenyl 2,4-dichlorophenyl ether
CN 5-Chloro-2-(2,4-dichlorophenoxy)phenol
CN Aquasept
CN Bacti-Stat soap
CN Cansan TCH
CN CH 3565
CN CH 3635
CN DP 300
CN Gamophen
CN Irgacare MP
CN Irgacide LP 10
CN Irgaguard B 1000
CN Irgaguard B 1325
CN Irgasan
CN Irgasan CH 3565
CN Irgasan DP 30
CN Irgasan DP 300
CN Irgasan DP 3000
CN Irgasan DP 400
CN Irgasan PE 30
CN Irgasan PG 60
CN Microban Additive B
CN Microban B
CN NM 100
CN Oletron
CN Sanitized XTX
CN Sapoderm
CN SterZac
CN TCCP
CN THDP
CN Tinosan AM 100
CN Tinosan AM 110
CN Triclosan
CN Ultra Fresh NM 100
CN Ultrafresh NM-V 2
CN Vinyzene DP 7000
CN Yujiexin
CN Zilesan UW
DR 164325-69-3, 112099-35-1, 88032-08-0, 261921-78-2
MF C12 H7 Cl3 O2
CI COM
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSDRUGNEWS, IMSPRODUCT, IPA, MEDLINE, MRCK*, MSDS-OHS, PIRA, PROMT, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, USPATOLD, VETU

(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3343 REFERENCES IN FILE CA (1907 TO DATE)
63 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
3357 REFERENCES IN FILE CAPLUS (1907 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> FIL MEDICINE
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	16.53	16.74

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CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 12:14:55 ON 20 SEP 2008
CA INDEXING COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

=> s l1
L2   13207 L1

=> s triclosan
L3   19219 TRICLOSAN

=> s l2 or l3
L4   21003 L2 OR L3

=> s malaria?
L5   357840 MALARIA?

=> s antimalaria?
L6   124642 ANTIMALARIA?

=> s l5 or l6
L7   408372 L5 OR L6

=> s l4 and l7
L8   474 L4 AND L7

=> s falciparum or berghei
L9   207454 FALCIPARUM OR BERGHEI

=> s l8 and l9
L10   312 L8 AND L9

=> s l10 an dl9
MISSING OPERATOR L10 AN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l9 an dl10
MISSING OPERATOR L9 AN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

```
=> d his

     (FILE 'HOME' ENTERED AT 12:12:49 ON 20 SEP 2008)

     FILE 'REGISTRY' ENTERED AT 12:13:14 ON 20 SEP 2008
L1              5 S TRICLOSAN

     FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CAPLUS, DDFB,
     DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ESBIOBASE,
     IFIPAT, IMSDRUGNEWS, IMSPRODUCT, IPA, KOSMET, LIFESCI, MEDLINE,
     NAPRALERT, NLDB, NUTRACEUT, PASCAL, PCTGEN, PHARMAML, ...' ENTERED AT
     12:14:55 ON 20 SEP 2008
L2          13207 S L1
L3          19219 S TRICLOSAN
L4          21003 S L2 OR L3
L5         357840 S MALARIA?
L6         124642 S ANTIMALARIA?
L7         408372 S L5 OR L6
L8            474 S L4 AND L7
L9         207454 S FALCIPARUM OR BERGHEI
L10           312 S L8 AND L9

=> s triclosan/ab
'AB' IS NOT A VALID FIELD CODE
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L11          6149 TRICLOSAN/AB

=> s l10 and l11
L12           166 L10 AND L11

=> s quinine or atabrine or chloroquine or mefloquine or primaquine or artemisinin or
artemether or artesunate
L13        217939 QUININE OR ATABRINE OR CHLOROQUINE OR MEFLOQUINE OR PRIMAQUINE
                  OR ARTEMISININ OR ARTEMETHER OR ARTESUNATE

=> s l12 and l13
L14            22 L12 AND L13

=> dup rem
```

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ENTER L# LIST OR (END):122
L22 IS NOT VALID HERE
The L-number entered has not been defined in this session, or it has been deleted. To see the L-numbers currently defined in this session, enter DISPLAY HISTORY at an arrow prompt (=>).

=> dup rem
ENTER L# LIST OR (END):114
DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DGENE, DRUGMONOG2, IMSPRODUCT, KOSMET, NUTRACEUT, PCTGEN, PHARMAML, USGENE'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L14
L15 11 DUP REM L14 (11 DUPLICATES REMOVED)

=> d l15 1-11 ibib, kwic

L15 ANSWER 1 OF 11 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
DUPLICATE 1
ACCESSION NUMBER: 2007:278443 BIOSIS
DOCUMENT NUMBER: PREV200700251712
TITLE: Antiplasmodial interactions between artemisinin and triclosan or ketoconazole combinations against blood stages of Plasmodium falciparum in vitro.
AUTHOR(S): Mishra, Lokesh C.; Bhattacharya, Amit; Bhasin, Virendra K. [Reprint Author]
CORPORATE SOURCE: Univ Delhi, Dept Zool, N Campus Delhi Univ, Delhi 110007, India
virendrabhasin@hotmail.com
SOURCE: American Journal of Tropical Medicine and Hygiene, (MAR 2007) Vol. 76, No. 3, pp. 497-501.
CODEN: AJTHAB. ISSN: 0002-9637.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Apr 2007
Last Updated on STN: 24 Oct 2007
TI Antiplasmodial interactions between artemisinin and triclosan or ketoconazole combinations against blood stages of Plasmodium falciparum in vitro.
AB Emergence of drug-resistant Plasmodium fialciparum strains to conventional first-line antimalarial drugs has compelled many countries to reorient their drug policies to adopt arternisinin-based combination therapies (ACTs) for treatment of uncomplicated malaria. This has increased the demand of artemisinin, already a scarce commodity. Synthesis of artemisinin is not vet commercially viable. Extensive use of available ACTs will invariably lead to emergence of resistance to these combinations. Thus, there is need to search for new artemisinin-based synthetic, inexpensive, synergistic combinations to reduce dependence on artemisinin. In vitro cultures of P. falciparum provide an appropriate system for identification of such new combinations. We evaluated interactions of artemisinin with triclosan or ketoconazole against blood stages of P. falciparum by a fixed-ratio isobologram method. Artemisinin shows mild synergistic interaction with triclosan and slight to marked antagonism with ketoconazole in vitro. These antiplasimodial interactions, however, require confirmation using in vivo model systems.
IT . . .
Pharmacology; Parasitology; Hematology (Human Medicine, Medical Sciences)

IT Parts, Structures, & Systems of Organisms
blood: blood and lymphatics
IT Diseases
malaria: blood and lymphatic disease, infectious disease, parasitic disease, drug therapy
Malaria (MeSH)
IT Chemicals & Biochemicals
artemisinin: antiinfective-drug, antiparasitic-drug;
ketoconazole: antiinfective-drug, antifungal-drug; triclosan: antiinfective-drug, antiseptic/disinfectant-drug
ORGN . . .
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates
ORGN Classifier
Sporozoa 35400
Super Taxa
Protozoa; Invertebrata; Animalia
Organism Name
Plasmodium falciparum (species): parasite, strain-3D7
Taxa Notes
Animals, Invertebrates, Microorganisms, Protozoans
RN 63968-64-9 (artemisinin)
65277-42-1 (ketoconazole)
3380-34-5 (triclosan)

L15 ANSWER 2 OF 11 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2007126774 EMBASE
TITLE: Enoyl reductases as targets for the development of anti-tubercular and anti-malarial agents.
AUTHOR: Oliveira, J.S.; Vasconcelos, I.B.; Santos, Diogenes S. (correspondence); Basso, Luiz A.
CORPORATE SOURCE: Centro de Pesquisas em Biologia Molecular e Funcional, Faculdade de Biociencias, Pontificia Universidade Catolica do Rio Grande do Sul, Porto Alegre, RS, Brazil. luiz.basso@pucrs.br; diogenes@pucrs.br
AUTHOR: Moreira, I.S.
CORPORATE SOURCE: Departamento de Quimica Organica e Inorganica, Universidade Federal do Ceara, Fortaleza, CE, Brazil.
AUTHOR: Santos, Diogenes S. (correspondence)
CORPORATE SOURCE: Centro de Pesquisas em Biologia Molecular e Funcional, Faculdade de Biociencias, Pontificia Universidade Catcolica do Rio Grande do Sul, Porto Alegre, RS, Brazil. diogenes@pucrs.br
SOURCE: Current Drug Targets, (Mar 2007) Vol. 8, No. 3, pp. 399-411.
Refs: 139
ISSN: 1389-4501 CODEN: CDTUAU
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review; (Review)
FILE SEGMENT: 017 Public Health, Social Medicine and Epidemiology
030 Clinical and Experimental Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Apr 2007

09763499

Last Updated on STN: 17 Apr 2007

TI Enoyl reductases as targets for the development of anti-tubercular and anti-malarial agents.

AB Tuberculosis (TB) and Malaria are neglected diseases, which continue to be major causes of morbidity and mortality worldwide, killing together around 5 million people. . . the Type II fatty acid biosynthesis system, which elongates acyl fatty acid precursors of mycolic acids. M. tuberculosis and P. falciparum enoyl reductases are targets for the development of anti-tubercular and antimalarial agents. Here we present a brief description of the mechanism of action of, and resistance to, isoniazid. In addition, data on inhibition of mycobacterial and plasmodial enoyl reductases by triclosan are presented. We also describe recent efforts to develop inhibitors of M. tuberculosis and P. falciparum enoyl reductase enzyme activity. .COPYRGT. 2007 Bentham Science Publishers Ltd.

CT Medical Descriptors:
antibiotic resistance
chemical analysis
combination chemotherapy
cost of illness
drug mechanism
drug metabolism
drug structure
drug targeting
enzyme inhibition
fatty acid synthesis
genetic analysis
human
malaria: DM, disease management
malaria: DR, drug resistance
malaria: DT, drug therapy
malaria: EP, epidemiology
molecular weight
morbidity
mortality
Mycobacterium
Mycobacterium tuberculosis
nonhuman
Plasmodium falciparum
prescription
product development
review
structural gene
tuberculosis: DM, disease management
tuberculosis: DR, drug resistance
tuberculosis: DT, drug therapy
tuberculosis: EP, epidemiology
unspecified side effect: SI, side effect
amikacin: DT, drug therapy
aminosalicylic acid: DT, drug therapy
amodiaquine: AN, drug analysis
amodiaquine: CB, drug combination
amodiaquine: DT, drug therapy
*antimalarial agent: AE, adverse drug reaction
*antimalarial agent: DV, drug development
artemisinin: AN, drug analysis
artemisinin: CM, drug comparison
artemisinin: DT, drug therapy
artemisinin: PE, pharmacoeconomics
artesunate: AN, drug analysis

artesunate: CB, drug combination
artesunate: DT, drug therapy
chloroquine: AN, drug analysis
chloroquine: CB, drug combination
chloroquine: CM, drug comparison
chloroquine: DT, drug therapy
chloroquine: PE, pharmacoeconomics
cycloserine: DT, drug therapy
*enoyl acyl carrier protein reductase (NADH): EC, endogenous compound
ethambutol: CB, drug combination
ethambutol: DT, drug therapy
ethambutol: PD, . . . analysis
isoniazid: CB, drug combination
isoniazid: DT, drug therapy
isoniazid: PK, pharmacokinetics
isoniazid: PD, pharmacology
isoniazid derivative: AN, drug analysis
isoniazid derivative: PD, pharmacology
kanamycin: DT, drug therapy
mefloquine: AN, drug analysis
mefloquine: CB, drug combination
mefloquine: DT, drug therapy
mycolic acid: EC, endogenous compound
oxidoreductase: EC, endogenous compound
pyrazinamide: CB, drug combination
pyrazinamide: DT, drug therapy
pyrazinamide: PD, pharmacology
pyrimethamine: AN, drug analysis
pyrimethamine: CB, drug combination
pyrimethamine: IT, drug interaction
pyrimethamine: DT, drug therapy
pyrimethamine: PD, pharmacology
quinine: AN, drug analysis
quinine: DT, drug therapy
quinoline derived antiinfective agent: DT, drug therapy
rifampicin: CB, drug combination
rifampicin: DT, drug therapy
rifampicin: PD, pharmacology
streptomycin: CB, drug combination
streptomycin:. . . drug therapy
streptomycin: PD, pharmacology
sulfadoxine: AN, drug analysis
sulfadoxine: CB, drug combination
sulfadoxine: IT, drug interaction
sulfadoxine: DT, drug therapy
sulfadoxine: PD, pharmacology
thioester: EC, endogenous compound
triclosan: AN, drug analysis
triclosan: PD, pharmacology
*tuberculostatic agent: AE, adverse drug reaction
*tuberculostatic agent: DV, drug development
unindexed drug

RN (amikacin) 37517-28-5, 39831-55-5; (aminosalicylic acid) 133-10-8, 133-15-3, 28088-64-4, 51540-64-8, 65-49-6, 80702-32-5; (amodiaquine) 69-44-3, 86-42-0; (artemisinin) 63968-64-9; (artesunate) 82864-68-4, 88495-63-0; (chloroquine) 132-73-0, 3545-67-3, 50-63-5, 54-05-7; (cycloserine) 339-72-0, 68-39-3, 68-41-7; (enoyl acyl carrier protein reductase (NADH)) 37251-08-4; (ethambutol) 10054-05-4, 1070-11-7, 3577-94-4, 74-55-5; (ethionamide) 536-33-4; (fansidar) 37338-39-9; (isoniazid) 54-85-3, 62229-51-0, 65979-32-0; (kanamycin)

11025-66-4, 61230-38-4, 8063-07-8; (mefloquine) 51773-92-3, 53230-10-7; (mycolic acid) 37281-34-8; (oxidoreductase) 9035-73-8, 9035-82-9, 9037-80-3, 9055-15-6; (pyrazinamide) 98-96-4; (pyrimethamine) 53640-38-3, 58-14-0; (quinine) 130-89-2, 130-95-0, 14358-44-2, 549-48-4, 549-49-5, 60-93-5, 7549-43-1; (rifampicin) 13292-46-1; (streptomycin) 57-92-1; (sulfadoxine) 2447-57-6; (triclosan) 3380-34-5

L15 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2007:40291 CAPLUS
DOCUMENT NUMBER: 146:243322
TITLE: Inhibitors of nonhousekeeping functions of the apicoplast defy delayed death in Plasmodium falciparum
AUTHOR(S): Ramya, T. N. C.; Mishra, Satyendra; Karmodiya, Krishanpal; Surolia, Namita; Surolia, Avadhesha
CORPORATE SOURCE: Molecular Biophysics Unit, Indian Institute of Science, Bangalore, 560012, India
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CODEN: AMACCQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Inhibitors of nonhousekeeping functions of the apicoplast defy delayed death in Plasmodium falciparum

AB . . . demonstrate that antibiotics like clindamycin, chloramphenicol, and tetracycline, inhibitors of prokaryotic protein synthesis, invoke the delayed death phenotype in Plasmodium falciparum, too, as evident from a specific reduction of apicoplast genome copy number Interestingly, however, mols. like triclosan, cerulenin, fops, and NAS-91, inhibitors of the recently discovered fatty acid synthesis pathway, and succinyl acetone, an inhibitor of heme. . . apicoplast as the site of metabolic pathways, which are required for parasite survival, and thus subserve the development of novel antimalarial therapy.

ST apicoplast inhibitor antimalarial malaria Plasmodium falciparum

IT Antimalarials
Malaria
Plasmodium falciparum
(inhibitors of nonhousekeeping functions of apicoplast defy delayed death in Plasmodium falciparum)

IT 54-05-7, Chloroquine 56-75-7, Chloramphenicol 60-54-8, Tetracycline 66-81-9, Cycloheximide 111-11-5, Methyl octanoate 112-39-0, Methyl palmitate 244-54-2, Diphenylene iodonium 1077-27-6, S-Lipoic acid 1200-22-2 3380-34-5, Triclosan 12772-57-5, Radicicol 13292-46-1, Rifampin 17397-89-6, Cerulenin 18323-44-9, Clindamycin 50594-66-6, Acifluorfen 51568-18-4, Succinyl acetone 69335-91-7, Fluazifop 69806-34-4, Haloxyfop 76578-12-6, Quizalofop 642093-27-4, NAS 91
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors of nonhousekeeping functions of apicoplast defy delayed death in Plasmodium falciparum)

L15 ANSWER 4 OF 11 DISSABS COPYRIGHT (C) 2008 ProQuest Information and Learning Company; All Rights Reserved on STN
ACCESSION NUMBER: 2007:10710 DISSABS Order Number: AAI3221126

TITLE: Development and application of a rapid site-specific integration system in the malaria parasite Plasmodium falciparum
AUTHOR: Nkrumah, Louis John [Ph.D.]; Fidock, David A. [advisor]; Jacobs, William R., Jr. [advisor]
CORPORATE SOURCE: Yeshiva University (0266)
SOURCE: Dissertation Abstracts International, (2006) Vol. 67, No. 6B, p. 2953. Order No.: AAI3221126. 147 pages. ISBN: 978-0-542-74229-3.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English
ENTRY DATE: Entered STN: 20070226
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TI Development and application of a rapid site-specific integration system in the malaria parasite Plasmodium falciparum

AB The current transfection techniques for genomic integration and complementation studies in the malaria parasite, Plasmodium falciparum, are inefficient and labor-intensive. It takes 3-5 months to achieve genetic integration in the parasite, many of which result in. . . integration of the plasmid into undesired regions of the genome. We have developed an efficient, site-specific integration system in P. falciparum, which uses the Bxb1 mycobacteriophage integrase to rapidly catalyze recombination between an attP plasmid and a chromosomal attB site. Transfection of attB+ P. falciparum lines with the attP plasmid produced recombinant attB x attP parasites within 2-4 weeks. The integration was stable in the. . . compartments in the parasite.

We employed the integrase-mediated attB x attP integration system to test whether pfenr (Plasmodium falciparum enoyl-ACP reductase) is the target of the antimalarial agent triclosan. We generated transgenic P. falciparum parasites expressing the A217V mutant of pfenr that was previously reported to cause a 7000-fold decrease in triclosan binding affinity. However, the A217V mutation failed to confer resistance to triclosan in the parasites. Further studies revealed that neither pfenr transcript nor protein was detectable in the asexual stages of the parasite. Targeted disruption of pfenr in P. falciparum produced viable parasites with no growth defects. Our results suggest that pfenr is not essential in the asexual stages of P. falciparum, where triclosan has been reported to kill the parasites, and hence may not be the target of triclosan.

We used allelic exchange technique to investigate the role of PfNHE (P. falciparum sodium-proton exchanger) in quinine resistance. Replacing the endogenous 3' untranslated region (UTR) of pfnhe with a truncated 3'UTR resulted in under-expression of PfNHE and a subsequent 30% reduction in quinine resistance in recombinant P. falciparum clones. The decrease in quinine resistance was observed only in parasites that were already resistant to quinine, suggesting that PfNHE contributes to quinine resistance, but only in a genome context already conferring a basal level of quinine resistance.

L15 ANSWER 5 OF 11 USPATFULL on STN
ACCESSION NUMBER: 2005:164780 USPATFULL
TITLE: Triclosan dosage form
INVENTOR(S): Lotter, Antonie Philippus, Potchefstroom, SOUTH AFRICA
Du Preez, Jan Lourens, Potchefstroom, SOUTH AFRICA
Collins, Lindi-May, Potchefstroom, SOUTH AFRICA

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 20050142204	A1	20050630	
APPLICATION INFO.:	US 2003-489732	A1	20020918	(10)
	WO 2002-ZA145		20020918	

	NUMBER	DATE
PRIORITY INFORMATION:	ZA 2001-7414	20010918

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, LLP, 901 NEW YORK AVENUE, NW, WASHINGTON, DC, 20001-4413, US
NUMBER OF CLAIMS: 18
EXEMPLARY CLAIM: 1-35
LINE COUNT: 421
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

TI Triclosan dosage form

AB This invention relates to triclosan and more particularly to a dosage form of triclosan especially for use in the treatment, including prophylaxis, of malaria. This invention further relates to use of a triclosan emulsion or oil solution in the preparation of a composition for use in the treatment, including prophylaxis, of malaria. This invention also relates to a method of treating, including prophylaxis of malaria and the use of a triclosan emulsion or oil solution in such a method.

SUMM This invention relates to triclosan and more particularly to a dosage form of triclosan especially for use in the treatment, including prophylaxis, of malaria. This invention further relates to use of triclosan in the preparation of a composition for use in the treatment, including prophylaxis, of malaria. This invention also relates to a method of treating, including prophylaxis, of malaria and the use of triclosan in such a method.

SUMM Malaria remains a leading global health problem, despite considerable efforts to control the disease over several decades. Approximately 40% of the world's population live in malaria -endemic areas, with about 90% of cases and most deaths occurring in tropical Africa (Beeson et al., 2001:149). There are up. . . of which 1 million are child fatalities annually (WB, 2001). the majority of severe clinical disease is due to Plasmodium falciparum, the young children and pregnant women at highest risk (Beeson, et al., 2001:149).

SUMM Malaria also has a significant negative economic effect. Research shows that malaria-afflicted families are able to harvest only approximately 40% of their crops, compared with healthy families, suggesting a link between malaria and poverty. The direct and indirect costs of malaria in Africa alone are estimated to exceed US $2 billion per year, while it is believed that the disease could be controlled with a budget amounting to one-tenth of this amount. Malaria slows economic growth in African countries by an estimated 1.3% each year (MRC, 2001).

SUMM Malaria is caused by several species of the protozoan Plasmodium, of which P. vivas and P. falciparum are the most common. They all have complex life cycles involving both the Anopheles mosquito and the erythrocyte of the. . . host. In vivax, a persisting tissue phase continues to infect the blood at intervals for many years Thus, the ideal antimalarial should not only eradicate the microzoan from the blood, (i.e., to `suppress` the clinical attack) but from the tissues as well, to effect a "radical cure". The several

antimalarials differ in their point of interruption of the cycle of the parasite and in the type of malaria affected (Harvey, 1975:1154).

SUMM Antimalarial treatment has advanced considerably over the last four centuries. Cinchona imported from Peru in 1643 allowed European countries and their colonies some means of suppressing the disease, and the introduction of quinine in the 19th century, followed by pamaquine in 1926 and quinacrine (alabrine) in 1930, improved treatment somewhat (Harvey, 1975:1154).

SUMM When supplies of quinine were cut off in World War II, the US Office of Scientific Research and Development co-ordinated a study of about. . . old, synthetic compounds. Not only were the older German compounds "rediscovered", but also several new and superior agents (including amodiaquine, chloroquine, pentaquine, and primaquine) (Harvey, 1975:1154).

SUMM However, a major problem and disadvantage of the know drugs is the emergence and spread of antimalarial drug resistance. This makes the development of new drugs an important priority (Beeson et al., 2001:149). Resistance of the malaria parasite to chloroquine, one of the cheapest and previously most useful antimalarial agents, is now widespread. Similarly, resistance to the combination of sulphadoxine-pyrimethamine is extensive in Asia and growing in Africa. Resistance. . . in treatment of severe disease, is becoming a major problem in certain parts of Asia. Relatively newer drugs, such as mefloquine, halofantrine, atovaquone-proguanil and artemether-lumefantrine still show efficacy but have limitations such as high cost. Novel uses for old drugs, such as chlorguanil-dapsone, and artemisinin combination therapy offer definite possibilities for the near future, but still have regulatory, policy and implementation hurdles to jump (Beeson. . .

SUMM Triclosan is a well known broad spectrum antibacterial agent active against many organisms. It has been in use as an antimicrobial. . . been done, and it was proven to be safe topically as well as orally (Bhargava, H. & Leonard, P. A., Triclosan: Application and safety, American Journal of Infection Control, vol. 24, no. 3, June 1996).

SUMM Surolia (Surolia, N & Surolia A, Nature Medicine, vol. 7, no. 2 February 2001, p 167-173) showed that triclosan is active against malaria parasites. However, they state that it would be a long time before an oral dosage form is developed. It has. . . Beeson et al. (Beeson, J. G., Winstanely, P. A., McFadden, G. I. & Brown, G. V. New agents to combat malaria. Nature Medicine, vol. 7, no. 2 February 2001, p. 149-150) states that a lot of work is still to be done before the product will be of use. A major disadvantage of triclosan is its very low solubility in water which has a detrimental influence on its absorption and thus its bioavailability. Although extensive toxicity studies have been done, and triclosan has been proven safe for oral use, it has not yet been formulated for this route.

SUMM It is therefore an object of the present invention to provide a dosage form of triclosan especially for the treatment, including prophylactic treatment, of malaria with which the aforesaid problems and disadvantages can be overcome or at least alleviated. Further objects of the invention are to provide use of triclosan in the preparation of a composition for use in the treatment, including prophylaxis, of malaria, a method of treating, including prophylaxis, of malaria and the use of triclosan in such a method, with which the aforesaid problems and disadvantages can be overcome or at least alleviated.

SUMM According to the present invention there is provided use of a

triclosan oil solution and/or triclosan emulsion in the preparation of a composition for use in the treatment, including prophylaxis, of malaria.

SUMM According to another aspect of the present invention there is provided a triclosan oil solution and/or triclosan emulsion for use in the treatment, including prophylaxis, of malaria.

SUMM According to yet another aspect of the present invention there is provided an anti-malaria dosage form comprising a triclosan oil solution and/or triclosan emulsion.

SUMM According to yet another aspect of the present invention there is provided the use of a triclosan oil solution and/or triclosan emulsion in the treatment, including prophylaxis, of malaria.

SUMM According to yet another aspect of the invention there is provided a method of manufacturing an anti-malaria dosage form including the steps of encapsulating triclosan in a form selected from the group consisting of an emulsion and an oil solution.

SUMM The triclosan may be dissolved or emulsified prior to encapsulation in a pharmacological acceptable oil selected from the group consisting of non-mineral. . .

SUMM The method may include the step of adding prior to encapsulation to the said triclosan form other formulation agents selected from the group consisting of anti-oxidants, BHA, surfactants, emulsifiers, preservatives, masking agents, sweeteners and combinations. . .

SUMM . . . to yet another aspect of the present invention there is provided a method of treating a human or animal against malaria by administering a triclosan oil solution and/or emulsion to the human or animal. The treatment may also include prophylactic treatment.

SUMM In one embodiment of the invention the triclosan is provided in the form of a triclosan oil solution. The triclosan may be dissolved in any suitable pharmacological acceptable oil, preferably a non-mineral oil. The non-mineral oil may comprise an animal. . .

SUMM In another embodiment of the invention the triclosan may be provided in the form of a triclosan emulsion. Any suitable triclosan emulsion may be used. In one embodiment of the invention the emulsion comprises an oil-in-water emulsion. The oil may comprise. . .

SUMM The triclosan oil solution and/or emulsion may be encapsulated, and this is especially the case where the triclosan is dissolved in a pharmacological acceptable oil. It appears that triclosan is very soluble in oils but has a bad taste at high concentration. The oily solution of triclosan may therefore not be acceptable to patients when administered as such and encapsulation should solve this problem. Preliminary studies have also shown that triclosan emulsions have a bad taste and that encapsulation of the emulsion may also be considered. The composition may be microencapsulated. . .

SUMM The triclosan oil solution and/or emulsion may be taken orally and in such a case the dosage form preferably comprises an encapsulated triclosan oil solution and/or emulsion. It is believed that when administered orally especially as capsules, the triclosan oil solution and/or emulsion may be effectively absorbed via the lymph system.

SUMM The triclosan oil solution and/or suspension may also include other formulation agents. For example in the case where an oil is used. . . a solvent an anti-oxidant like BHA may be used to prevent oxidation of the oil. In the case of the triclosan suspension, surfactants, which serve as emulsifiers may be used. Preservatives and

masking agents such as sweeteners may also be employed.

DETD Triclosan Oil Solution for Encapsulation

DETD Triclosan in the amount of 100 g was mixed with 200 g of sunflower oil with slight heating (up to 60° C.) until it dissolved. The solution was left to cool and de-aerate. Soft gelatin capsules of the triclosan oil solution were then prepared.

DETD Triclosan Emulsion

DETD The following compounds were used to prepare a high concentration triclosan emulsion:

Triclosan	16 g
Sunflower oil	34 g
BHA	0.01 g
Span 80	5 g
Tween 80	5 g
Methyl paraben	0.1. . .

DETD The triclosan was weighed and dissolved in the sunflower oil while stirring over low heat (up to 60° C.). When all the triclosan had dissolved, the BHA, Span 80, Tween 90 and preservatives were added. Na-saccharin was dissolved in a little warm water.. . .

DETD The Assessment of the Bioavailability of Triclosan Dosage Forms

DETD HPLC Method for the Determination of Triclosan in Blood

DETD . . .

Injection volume: 100 μl.

Detection: UV at 210 nm.

Retention time: Approximately 5.1 and 6.3 minutes for triclosan and acenaphthene respectively.

Solvent: methanol.

DETD D) Standard Solution:

1. Weigh approximately 20 mg of triclosan accurately and dissolve in 250 ml of solvent.

2. Make further dilutions of 5 ml to 100 ml and. . .

DETD Surolia and Surolia (2001:168) state that 3 μM (580 ng/ml) triclosan is sufficient for 50% inhibition of fatty acid synthesis in Plasmodium falciparum. One must assume that this includes triclosan in both the conjugated and unconjugated form.

DETD Results and Discussion

TABLE 1

Total triclosan in Plasma					
	subject no.				
	1	2	3	4	Mean
Time (hours)	ng/ml				
0	0	0	0	0	0
0.333	248	1468	1622	1218. . .	

DETD As can be seen from tables 1 and 2 as well as FIG. 1, triclosan was released from the soft gelatine capsules and absorbed. The bioavailability was good in three of the four volunteers. The. . .

DETD Triclosan concentrations as high as 22000 ng/ml (22 μg/ml) was found in plasma, which is about 30 times higher than the. . .

DETD The applicant has therefore found that triclosan in the form of any emulsion or an oil solution is an effective composition and dosage form for the treatment, including prophylaxis, of malaria

. However, it will be appreciated that many variations in detail are possible with a dosage form of triclosan, the use of triclosan, a method of treating malaria according to the invention without departing from the scope of the appended claims. For example, the triclosan could be dissolved or emulsified in a pharmacological acceptable oil selected from the group consisting of non-mineral oils, animal derived. . . oils, plant derived oils, sunflower oil, olive oil, arachis oil, and sesame oil, and mixtures thereof. Further for example, the triclosan form could include other formulation agents selected from the group consisting of anti-oxidants, BHA, surfactants, emulsifiers, preservatives, masking agents, sweeteners and combinations thereof. Even further for example, the triclosan form could be encapsulated or microencapsulated. Yet further for example, the triclosan form could be prepared in the form of soft gelatin capsules.

DETD 1. BEESON, J. G., WINSTANLEY, P. A., MCFADDEN, G. I. & BROWN, G. V. 2001. New agents to combat malaria. Nature medicine (7(2):149-150, February.

DETD 3. MRC (Medical Research Council, South Africa). 2001. General information on malaria. Available on Internet: http://www.malaria.org.za/Malaria_Risk/General_Information/general_inf ormation.htm

DETD 5. SCHULZE, J., MARQUARDT, F., LYMAN, F. & SPITZER, C. 1974. Determination of free and conjugated triclosan in blood by electron capture gas liquid chromatography. Journal of the American Oil Chemists' Society, 52:215-218.

DETD 6. SUROLIA, N. AND SUROLIA, A. 2001. Triclosan offers protection against blood stages of malaria by inhibiting enoyl-ACP reductase of Plasmodium falciparum. Nature medicine, 7(2):167-173, February.

DETD 7. WB (World Bank). 2001. Malaria at a glance. Available on Internet: http://www.rbm.who.int [Date of use: Aug. 24, 2001].

CLM What is claimed is:
36. A method of manufacturing an oral anti-malaria dosage form including the steps of encapsulating triclosan in a form selected from the group consisting of an emulsion and an oil solution.

CLM What is claimed is:
37. A method according to claim 36 wherein the triclosan is dissolved or emulsified prior to encapsulation in a pharmacological acceptable oil selected from the group consisting of non-mineral oils,. . .

CLM What is claimed is:
. . . A method according to claim 36 or claim 37 including the step of adding prior to encapsulation to the said triclosan form other formulation agents selected from the group consisting of anti-oxidants, BHA, surfactants, emulsifiers, preservatives, masking agents, sweeteners and combinations. . . .

CLM What is claimed is:
39. Triclosan in an encapsulated dosage form selected from the group consisting of an emulsion and an oil solution for use in the oral treatment, including prophylaxis, of malaria.

CLM What is claimed is:
40. Triclosan according to claim 39 which is dissolved or emulsified in a pharmacological acceptable oil selected from the group consisting of. . .

CLM What is claimed is:
41. Triclosan according to claim 39 or claim 40 in combination with formulation agents selected from the group consisting of

anti-oxidants, BHA,. . .

CLM What is claimed is:
42. Triclosan according to claim 39 which is microencapsulated.

CLM What is claimed is:
43. Triclosan according to claim 39 which is prepared as soft gelatin capsules.

CLM What is claimed is:
44. An anti-malaria oral dosage form comprising triclosan in a form selected from the group consisting of an emulsion and an oil solution in a pharmaceutically acceptable encapsulation. . .

CLM What is claimed is:
45. An anti-malaria oral dosage form according to claim 44 wherein the triclosan is dissolved or emulsified in a pharmacological acceptable oil selected from the group consisting of non-mineral oils, animal derived oils,. . .

CLM What is claimed is:
46. An anti-malaria dosage form according to claim 44 or claim 45 wherein the said triclosan form includes other formulation agents selected from the group consisting of anti-oxidants, BHA, surfactants, emulsifiers, preservatives, masking agents, sweeteners and. . .

CLM What is claimed is:
47. A method of orally treating a human or animal against malaria by administering a pharmaceutically effective amount of triclosan in an oral dosage form selected from the group consisting of an emulsion and an oil solution to the human. . .

CLM What is claimed is:
48. A method according to claim 47 wherein the triclosan is dissolved or emulsified in a pharmacological acceptable oil selected from the group consisting of non-mineral oils, animal derived oils,. . .

CLM What is claimed is:
49. A method according to claim 47 or claim 48 wherein the said triclosan form includes other formulation agents selected from the group consisting of anti-oxidants, BHA, surfactants, emulsifiers, preservatives, masking agents, sweeteners and. . .

CLM What is claimed is:
50. A method according to claim 47 wherein the said triclosan form is microencapsulated.

CLM What is claimed is:
51. A method according to claim 47 wherein the said triclosan form is prepared as soft gelatin capsules.

IT 3380-34-5, Triclosan
(triclosan dosage forms for malaria treatment)

L15 ANSWER 6 OF 11 USPATFULL on STN
ACCESSION NUMBER: 2004:178280 USPATFULL
TITLE: Fab I and inhibition of apicomplexan parasites
INVENTOR(S): McLeod, Rima, Chicago, IL, UNITED STATES
Muench, Stephen P., Stockport, UNITED KINGDOM
Rafferty, John B., Sheffield, UNITED KINGDOM
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Mack, Douglas G., Centennial, CO, UNITED STATES
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Prigge, Sean, Severna Park, MD, UNITED STATES
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	NUMBER	KIND	DATE
PATENT INFORMATION:	US 20040137446	A1	20040715
APPLICATION INFO.:	US 2003-465527	A1	20030618 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	WO 2001-US49738	20011220

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BARNES & THORNBURG, P.O. BOX 2786, CHICAGO, IL, 60690-2786
NUMBER OF CLAIMS: 9
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 17 Drawing Page(s)
LINE COUNT: 764
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Discovery and characterization of an apicomplexan Fab I gene and encoded enzyme and discovery of the triclosan as a lead compound, provide means to rationally design novel inhibitory compositions useful for prevention and treatment of apicomplexan related. . .

SUMM [0001] Discovery and characterization of an apicomplexan Fab I gene and encoded enzyme and the discovery of triclosan as a lead compound, provide means to rationally design novel inhibitory compositions useful for prevention and treatment of apicomplexan and. . .

SUMM [0003] Apicomplexan infections are among the most common and devastating infectious diseases. Malaria (Plasmodium) kills one child every eleven seconds and three million people every year. It is a cause of substantial morbidity. . .

SUMM . . . al., 1998; Waller et al., 1998; Zuther et al., 1999; Payne et al., 2000). Notably, both T. gondii and P. falciparum have been shown to possess mono-functional, plant- or bacterial-like fatty acid biosynthesis enzymes which are targeted to the plastid organelle. . .

SUMM . . . on the inhibition of ENR by compounds such as the diazaborines (Turnowsky et al., 1989; Baldock et al., 1996) and triclosan (McMurray et al., 1998; Heath et al., 1998; Levy et al., 1999; Payne et al., 2000; and Jones et al., 2000) have validated this enzyme as a target for the development of new antibacterial agents. In particular, triclosan, which is found in many house-hold formulations including soaps, deodorants, hand lotion, toothpaste and impregnated into plastics as an anti-bacterial. . .

SUMM . . . invention relates the first report of apicomplexan Fab I (enoyl acyl carrier protein reductase, ENR) and discloses the effects of triclosan, a potent and specific inhibitor of this enzyme, on the in vitro growth of T. gondii and P. falciparum chain. A plant-like Fab I in P. falciparum was identified by the inventors and the structure was modeled on the Brassia napus and Escherichia coli structures, alone and complexed to triclosan (5-chloro-2-[2,4 dichloropheoxyl] phenol), which confirmed all the requisite features of an enoyl acyl carrier protein reductase (ENR) and

its interactions with triclosan. Like the remarkable effect of triclosan on a wide variety of bacteria, this compound markedly inhibits growth and survival of the apicomplexan parasites P. falciparum and Toxoplasma gondii at low concentrations (i.e., IC50.congruent.150-2000 and 62 nanogram/ml respectively).

SUMM [0007] Initially, a sequence for a putative Plasmodium falciparum Fab I was located on the aggregate P. falciparum chromosomes referred to as "blob" (GenBank Accession Number AF338731). The deduced amino acid sequence and a multisequence alignment with representative. . . . obtained with a BLAST search using the sequences from both the B. napus and E. coli enzymes within the P. falciparum database "PlasmoDB" (found at www.PlasmoDB.org). (See Materials and Methods). This sequence was then converted to an amino acid sequence at. . .

SUMM . . . Interestingly, there is much greater sequence similarity with the plant enzyme than with the ENRs of bacterial origin. The P. falciparum enoyl acyl carrier protein reductase appears to have a plastid targeting sequence (Waller et al., 2000) and has a number of internal insertions. In addition, the P. falciparum protein has an extremely polar additional internal insertion for which no counterpart exists in any of the previously described enoyl. . .

SUMM [0010] Because Fab I was located, the effects of triclosan on Plasmodium falciparum in vitro were investigated. For P. falciparum, the in vitro assays (Milhous et al., 1985; Oduola et al., 1988) were conducted using a modification of the semiautomated. . . N2 for 48 h. [3H]-Hypoxanthine incorporation was measured as described previously (Milhous et al, 1985; Oduola et al, 1988). P. falciparum strain W2 is susceptible to mefloquine, but resistant to pyrimethamine, sulphadoxine and quinine and less susceptible to chloroquine than P. falciparum strain D6. Strain D6 is susceptible to pyrimethamine and sulphadoxine, but similar to P. falciparum strains TM90C2A and TM90C2B, and strain TM91C235 is less susceptible to mefloquine.

SUMM [0011] The effect of triclosan on P. falciparum in vitro was studied with pyrimethamine sensitive and resistant organisms, and those with varying sensitivity to chloroquine and mefloquine, simultaneously with studies of effect of chloroquin or mefloquine on these parasites (Table 1). Triclosan was effective against pyrimethamine resistant P. falciparum (W2) at low concentrations (IC50s of 150 nanograms/ml [triclosan] and 160 ngm/ml [Chloroquin], respectively) (Table 1). Interestingly, the pattern of relative susceptibility of triclosan and mefloquine were identical. This similarity suggests that triclosan and mefloquine may share a common mechanism of influx or efflux, because such differences in transporters are believed to be the basis of the differences in susceptibility of malaria parasites to mefloquin although other mechanisms are possible.

SUMM [0014] Triclosan also was effective against T. gondii, in nanomolar amounts (FIG. 2). IC50 was 62 nanograms/ml. There was no toxicity to. . .

SUMM [0015] Analysis of the binding site for triclosan in B. napus and E. coli ENR shows that 11 residues have contacts less than 4 Å with one of more atoms of the triclosan (FIG. 3). Inspection of the sequence for P. falciparum ENR reveals that it shares sequence identity at each of these positions with either the sequence of the B. napus or E. coli enzymes providing a clear explanation for the inhibitory properties of this agent against P. falciparum.

SUMM [0016] The discovery and characterization of an apicomplexan Fab I and discovery of triclosan as a lead compound provide means to

rationally design novel inhibitory compounds with considerable promise. The invention provides novel ways to counteract the increasing resistance of Plasmodium to the current armoury of antimalarial agents and provides a new approach to the great need for additional, less toxic antimicrobial agents effective against T. gondii.. . . other novel inhibitors of sequential enzymatic steps in the apicomplexan lipid synthesis pathway, that are predicted to be synergistic with triclosan and other inhibitors of Fab I (Baldock, et al., 1996). This also raises the exciting possibility of a rational basis. . .

DRWD . . . shows a multiple structure-based sequence alignment of the enoyl reductases from E. coli, H. pylori, B. subtilis, S. aureus, P. falciparum and B. napus. The secondary structures and sequence numbers of the E. coli and B. napus enzymes are shown above. . . . the alignment, respectively. The residues which are completely conserved are all black with white faced type and those involved in triclosan binding are indicated with a black, filled circle above. The N terminal sequence in the P. falciparum Fab I with no corresponding sequence in E. coli is a plastid target sequence which is a suitable separate target. . .

DRWD [0018] FIG. 2 demonstrates inhibition of T. gondii by triclosan . (a) no inhibitory effect of triclosan on the host cells uptake of thymidine; appearance of the monolayer also was unchanged. (b) effect of triclosan on T. gondii uracil uptake; triclosan reduces uracil uptake by intracellular T. gondii 4 days after infection; IC50 was .congruent.62 nanograms per ml; effect increased between days 1 to 4, for example, in a separate experiment, for 125 nanograms per ml of triclosan on day 1, percentage inhibition was 20% and on day 4 was 72% and for pyrimethamine/sulfadiazine percentages of inhibition at. . .

DRWD . . . FIG. 3 is a stereo view of the three dimensional arrangement of the atoms that form the binding pocket for triclosan, in E. coli enoyl reductase, with the 11 residues that have any atom within 4 Å of the inhibitor, labeled. This is important in assigning the relative contributions made to the interaction with triclosan by the critical amino acids that are also present in the P. falciparum enzyme.

DRWD . . . activity by 1 mM glyosate. Squares, without glyphosate. Circles, with glyphosate; (E) shows evidence for the shikimate pathway in P. falciparum with functional evidence for the shikimate pathway in P. falciparum. Glyphosate inhibition of in vitro growth of asexual erythrocytic forms and PABA and folate antagonism of growth inhibition. Effect of. . .

DRWD [0025] FIG. 9 is an illustrative copy of a web page for the Plasmodium falciparum genomic sequence.

DRWD [0029] FIG. 13 shows a model of triclosan binding to its target enzyme, ENR.

DRWD [0031] FIG. 15 is the molecular formula and model for triclosan .

DETD [0032] A plant-like FAB I was identified in Plasmodium falciparum. The nucleotide sequence and deduced amino acid sequence was prepared and correct sequences were confirmed. FAB I is a single chain, discrete enzyme. All requisite residues for FAB I enzyme activity were confirmed. The P. falciparum enayl acyl carrier protein reductase has a putative plastid targeting sequence and unique polar insertions. The FAB I structure is modeled on E. coli and B. napus FAB I structure alone and complexed to triclosan. Key amino acids were identified for 2° structure. Residues for binding triclosan were conserved providing explanation for inhibition by triclosan. Triclosan inhibits P. falciparum, T. gondii (nm) in a pattern similar to the action of mefloquine

. Soluble protein can be overexpressed.

DETD [0033] Information obtained from P. falciparum because FAB I was purified include that the N terminal sequence is the same as B. napus FAB I, enzyme activity is NADH dependent and inhibited by triclosan. FAB I is involved in synthesis of 10, 12 C fatty acids. In a P. berghei murine model, Triclosan administered subcutaneously (3 or 38 mg/kg) was nontoxic, cleared parasitemia and prevented death. Synergy was demonstrated in vitro with cerulein,. . .

DETD [0036] P. falciparum. The in vitro assays (Oduala et al., 1988; Milhous et al., 1985) were conducted using a modification of the semiautomated. . . . 5% CO2 and 90% N2 for 48h, [3H]-Hypoxanthine incorporation was measured as described previously (13, 14). W2 is susceptible to mefloquine, but resistant to pyrimethamine, sulphadoxine, but similar to TM90C2A and TM90C2B, and TM91C235 is less susceptible to mefloquin.

DETD [0037] TABLE 1: IC 50.sup.1 OF Triclosan, Chloroquine , AND Mefloquine When Cultured with P Falciparum (Nanograms/Ml)

DETD [0038] The activity of triclosan, mefloquine, and chloroquine were tested against a series of P. falciparum isolates and clones with differing susceptibilities to antimalarial drugs. D6, a clone from the African Sierra I/UNC isolate, is chloroquine and pyrimethamine susceptible; W2 is a clone of the Indochina I isolate and is chloroquine and pyrimethamine resistant. TM90C2A, TM90C2B, and TM91C235 are isolates from Thailand and all are chloroquine and mefloquine resistant. TM91C235 was isolated from a patient that failed mefloquine twice, whereas TM90-C2a and TM90-Cb are admission and recrudescent isolates, respectively, of the first patient who failed treatment with atovaquone. . . atovaquone, when compared with the admission isolate and other atovaquone--susceptible isolates from Thailand.

Antimicrobial Agents	Parasite Strain D6	TM90C2A	W2	TM90C2B	TM91C235
Triclosan	387.1	1891.4	154.4	1330.4	1800.5
Mefloquine	5.3	24.5	2.0	19.3	19.6
Chloroquine	3.8	57.3	162.4	82.7	46.1

DETD [0039] Cloning of the FabI gene. The FabI gene from Plasmodium falciparum is located on chromosome 4 and codes for a 432 amino acid protein. The FabI gene from gDNA of the 3D7 strain of P. falciparum was amplified using Pfu Turbo polymerase (Stratagene) and two primers (5'-GGTGGTGAATTCATGAATAAAATATCACAACGG-3' and 5'-GGTGGTGTCGACTTATTCATTTTCATTGCGATATATATC-3'). The resulting amplicon was digested with EcoRI. . . .

DETD [0043] Overexpression of Recombinant Fab I. The FabI gene was amplified from cDNA of the 3D7 strain of P. falciparum and inserted into the pMAL-c2x vector (New England Biolabs) for expression in E. coli. Recombinant FabI fused the Maltose Binding. . .

DETD . . . M., Zeidler J., Lichtenhaler H. K., Soldati D., Beck E., 1999. Inhibitors of the nonmevalonate pathway of isoprenoid biosynthesis as antimalarial drugs. Science. 285 (5433):1573-6.

DETD [0048] Jones R. D., Janpani H., Newman J. L., Lee A., 2000. Triclosan: A review of effectiveness and safety in healthcare settings. Am J. Inf. Control. 28, 184-196.

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Nature. 398, 383-384.
DETD [0051] McMurray L. M., Oethinger M., Levy S. B., 1998. Triclosan targets lipid synthesis. Nature. 394, 531-2.
DETD . . . Weatherly N. F., Bowdre J. H., Desjardins R. E., 1985. In vitro activities and mechanisms of resistance to anti-folates and anti-malarial drugs. Antimicrob. Agents Chemother. 27, 525-530.
DETD [0053] Oduola A. M. J., Weatherly N. J., Bowdre J. H., Desjardins R. E., 1988. Plasmodium falciparum--cloning by single erythrocyte micromanipulation and heterogeneity in vitro. Exp. Parasitol. 66, 86-95.
DETD [0055] Plasmodium Genome Database Collaborative, 2001. PlasmoDB: An integrative database of the P. falciparum genome. Tools for accessing and analyzing finished and unfinshed sequence data. Nucl. Acids Res. 29: 66-69.
DETD . . . G. S., Roos D. S., McFadden G. I., 1998. Nuclear-encoded proteins target to the plastid in Toxoplasma gondii and Plasmodium falciparum. Proc Natl Acad Sci USA. 95(21), 12352-12357.
DETD . . . Waller R. F., Reed M. D., Cowman A. F., McFadden G. I., 2000. Protein trafficking to the plastid of Plasmodium falciparum is via the secretory pathway. EMBO J.19(8): 1794-802.
DETD . . . J., Taylor, I. W. F., 1999. Kinetic and structural characteristics of the inhibition of enoyl (acyl carrier protein) reductase by triclosan. Biochemistry. 38, 12514-12525.
DETD SEQUENCE CHARACTERISTICS:
SEQ ID NO: 5
LENGTH: 420
TYPE: PRT
ORGANISM: Plasmodium falciparum
SEQUENCE: 5
Met Asn Lys Ile Ser Gln Arg Leu Leu Phe Leu Phe Leu His Phe Tyr
1 5 . .
CLM What is claimed is:
. . . 1. A molecule of the Fab I enzyme having the amino acid sequence of the Fab I enzyme in Plasmodium falciparum, as shown in FIG. 1.

CLM What is claimed is:
3. The use of claim 2, wherein the apicomplexan is Plasmodium falciparum.

CLM What is claimed is:
5. A novel recombinant protein with an amino acid sequence substantially similar to that of Plasmodium falciparum shown FIG. 1.

CLM What is claimed is:
8. Use of the plasmid targeting sequence of the Plasmodium falciparum Fab I amino acid sequence according to FIG. 1, to design antimicrobial agents and inhibitors of apicomplexan growth and survival.
. . . .
CLM What is claimed is:
9. Use of triclosan to inhibit apicomplexan growth and survival.

IT 3380-34-5, Triclosan
(as specific inhibitor of Fab I, use to inhibit apicomplexan growth and survival; cloning and sequencing of Plasmodium falciparum Fab I (enoyl acyl carrier protein reductase) gene and method for inhibition of apicomplexan parasites)

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DUPLICATE 3

09763499

ACCESSION NUMBER: 2004:409132 BIOSIS
DOCUMENT NUMBER: PREV200400410242
TITLE: The efficacy of inhibitors involved in spermidine metabolism in Plasmodium falciparum, Anopheles stephensi and Trypanosoma evansi.
AUTHOR(S): Moritz, E.; Seidensticker, S.; Gottwald, A.; Maier, W.; Hoerauf, A.; Njuguna, J. T.; Kaiser, A. [Reprint Author]
CORPORATE SOURCE: Inst Med Parasitol, Sigmund Freud Str 25, D-53105, Bonn, Germany
akaiser@parasit.meb.uni-bonn.de
SOURCE: Parasitology Research, (September 2004) Vol. 94, No. 1, pp. 37-48. print.
ISSN: 0932-0113 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 20 Oct 2004
Last Updated on STN: 20 Oct 2004

TI The efficacy of inhibitors involved in spermidine metabolism in Plasmodium falciparum, Anopheles stephensi and Trypanosoma evansi.

AB . . . have tested the effect of different polyamine inhibitors of the spermidine metabolizing enzymes deoxyhypusine synthase and homospermidine synthase in different chloroquine resistant Plasmodium falciparum strains, in the mosquito Anopheles stephensi (Diptera: Culicidae) and in a Trypanosoma evansi clone I from strain STIB 806 K China. Recent experiments have shown that agmatine is a growth inhibitor of the malaria parasite P. falciparum (Kaiser et al. 2001) in vitro. A comparison of agmatine efficacy with the new antimalarials artemisinin, triclosan and conventional chloroquine showed similar or even better results on the basis of growth inhibition and the reduction of developmental forms. However, no effect of triclosan or agmatine was observed at the ribonucleic acid level. In a second set of experiments, we tested the effect of. . .

IT . . .
and Lymphatics (Transport and Circulation); Infection; Parasitology; Pharmacology

IT Diseases
African sleeping sickness: parasitic disease, diagnosis, drug therapy

IT Diseases
malaria: blood and lymphatic disease, parasitic disease, diagnosis, drug therapy
Malaria (MeSH)

IT Chemicals & Biochemicals
1,3-diaminopropane: antiinfective-drug, antiparasitic-drug; 1,7-diaminoheptane: antiinfective-drug, antiparasitic-drug, antimalarial, deoxyhypusine inhibitor; 1,8-diaminooctane: antiinfective-drug, antiparasitic-drug; agmatine: antiinfective-drug, antiparasitic-drug, antimalarial, antisporozoite effect, efficacy, growth inhibitor; artemisinin: antiinfective-drug, antimalarial; chloroquine: antiinfective-drug, antiparasitic-drug, antimalarial; deoxyhypusine synthase [EC 2.5.1.46]; dicyclohexylamine: antiinfective-drug, antiparasitic-drug, antimalarial, spermidine biosynthesis inhibitor; homospermidine synthase [EC 2.5.1.44]; polyamine inhibitor; ribonucleic acid; spermidine: biosynthesis inhibition, metabolism inhibition; triclosan: antiinfective-drug, antiparasitic-drug, antimalarial

ORGN . . .
Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

ORGN Classifier
Sporozoa 35400
Super Taxa
Protozoa; Invertebrata; Animalia
Organism Name
Plasmodium falciparum (species): pathogen, oocyst, strain-Dd2, strain-NF54, strain-R
Taxa Notes
Animals, Invertebrates, Microorganisms, Protozoans
RN 109-76-2 (1,3-diaminopropane)
646-19-5 (1,7-diaminoheptane)
373-44-4 (1,8-diaminooctane)
306-60-5 (agmatine)
63968-64-9 (artemisinin)
54-05-7 (chloroquine)
127069-31-2 (deoxyhypusine synthase)
127069-31-2 (EC 2.5.1.46)
101-83-7 (dicyclohexylamine)
76106-84-8 (homospermidine synthase)
76106-84-8 (EC 2.5.1.44)
124-20-9 (spermidine)
3380-34-5 (triclosan)

L15 ANSWER 8 OF 11 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2003272093 EMBASE
TITLE: Targeting tuberculosis and malaria through inhibition of enoyl reductase. Compound activity and structural data.
AUTHOR: Kuo, Mack R.; Iwamoto, Hiroyuki; Perozzo, Remo; Sacchettini, James C. (correspondence)
CORPORATE SOURCE: Dept. of Biochem. and Biophysics, Texas A and M University, College Station, TX 77843, United States. sacchett@tamu.edu
AUTHOR: Morbidoni, Hector R.; Jacobs Jr., William R.; Fidock, David A.
CORPORATE SOURCE: Dept. of Microbiol. and Immunology, Bronx, NY 10461, United States.
AUTHOR: Jacobs Jr., William R.
CORPORATE SOURCE: Howard Hughes Medical Institute, Albert Einstein College of Medicine, Bronx, NY 10461, United States.
AUTHOR: Alland, David
CORPORATE SOURCE: Division of Infectious Diseases, Center for Emerging Pathogens, New Jersey Medical School, Newark, NJ 07103, United States.
AUTHOR: Sneddon, Scott F.; Gourlie, Brian B.; Staveski, Mark M.; Leonard, Marina; Gregory, Jill S.; Janjigian, Andrew D.; Yee, Christopher
CORPORATE SOURCE: Genzyme Drug Discovery, Genzyme Corp., Cambridge, MA 02139-1562, United States.
AUTHOR: Musser, James M.
CORPORATE SOURCE: Lab. of Human Bact. Pathogenesis, Division of Intramural Research, National Institutes of Health, Hamilton, MT 59840, United States.
AUTHOR: Kreiswirth, Barry
CORPORATE SOURCE: Pub. Hlth. Res. Institute TB Center, New York, NY 10016, United States.
AUTHOR: Sacchettini, James C. (correspondence)
CORPORATE SOURCE: Dept. of Biochem. and Biophysics, Texas A and M University, Biochemistry and Biophysics Bldg., College Station, TX 77843, United States. sacchett@tamu.edu

SOURCE: Journal of Biological Chemistry, (6 Jun 2003) Vol. 278, No. 23, pp. 20851-20859.
Refs: 46
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 24 Jul 2003
Last Updated on STN: 24 Jul 2003

TI Targeting tuberculosis and malaria through inhibition of enoyl reductase. Compound activity and structural data.

AB Tuberculosis and malaria together result in an estimated 5 million deaths annually. The spread of multidrug resistance in the most pathogenic causative agents, Mycobacterium tuberculosis and Plasmodium falciparum, underscores the need to identify active compounds with novel inhibitory properties. Although genetically unrelated, both organisms use a type II. . . with a combinatorial library, we have identified two novel classes of compounds with activity against the M. tuberculosis and P. falciparum enzyme (referred to as InhA and PfENR, respectively). The crystal structure of InhA complexed with NAD(+) and one of the inhibitors was determined to elucidate the mode of binding. Structural analysis of InhA with the broad spectrum antimicrobial triclosan revealed a unique stoichiometry where the enzyme contained either a single triclosan molecule, in a configuration typical of other bacterial ENR:triclosan structures, or harbored two triclosan molecules bound to the active site. Significantly, these compounds do not require activation and are effective against wild-type and drug-resistant strains of M. tuberculosis and P. falciparum. Moreover, they provide broader chemical diversity and elucidate key elements of inhibitor binding to InhA for subsequent chemical optimization.

CT Medical Descriptors:
article
bacterial growth
crystal structure
drug structure
enzyme active site
*enzyme inhibition
*malaria
minimum inhibitory concentration
Mycobacterium tuberculosis
nonhuman
Plasmodium falciparum
priority journal
stoichiometry
structure analysis
*tuberculosis
antiinfective agent: AN, drug analysis
carrier protein: EC, endogenous compound
chloroquine: CM, drug comparison
cycloguanil: CM, drug comparison
*enoyl acyl carrier protein reductase: CM, drug comparison
*enoyl acyl carrier protein reductase: DV, drug development
*enoyl. . . 8575: DV, drug development
*genz 8575: PD, pharmacology

isoniazid
*protein inhA: CM, drug comparison
*protein inhA: DV, drug development
*protein inhA: PD, pharmacology
pyrimethamine: CM, drug comparison
quinine: CM, drug comparison
sulfadoxine: CM, drug comparison
triclosan: AN, drug analysis
unclassified drug
RN (carrier protein) 80700-39-6; (chloroquine) 132-73-0, 3545-67-3, 50-63-5, 54-05-7; (cycloguanil) 516-21-2; (fatty acid synthase) 9045-77-6; (isoniazid) 54-85-3, 62229-51-0, 65979-32-0; (pyrimethamine) 53640-38-3, 58-14-0; (quinine) 130-89-2, 130-95-0, 14358-44-2, 549-48-4, 549-49-5, 60-93-5, 7549-43-1; (sulfadoxine) 2447-57-6; (triclosan) 3380-34-5

L15 ANSWER 9 OF 11 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2002309077 EMBASE
TITLE: Structural elucidation of the specificity of the antibacterial agent triclosan for malarial enoyl acyl carrier protein reductase.
AUTHOR: Perozzo, Remo; Kuo, Mack; Sidhu, Amar bir Singh; Valiyaveettil, Jacob T.; Bittman, Robert; Jacobs Jr., William R.; Fidock, David A.; Sacchettini, James C. (correspondence)
CORPORATE SOURCE: Department of Biochemistry, Texas A and M University, College Station, TX 77843-2128, United States. sacchett@tamu.edu
SOURCE: Journal of Biological Chemistry, (12 Apr 2002) Vol. 277, No. 15, pp. 13106-13114.
Refs: 62
ISSN: 0021-9258 CODEN: JBCHA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Sep 2002
Last Updated on STN: 19 Sep 2002
TI Structural elucidation of the specificity of the antibacterial agent triclosan for malarial enoyl acyl carrier protein reductase.
AB The human malaria parasite Plasmodium falciparum synthesizes fatty acids using a type II pathway that is absent in humans. The final step in fatty acid elongation. . . . enoyl acyl carrier protein reductase, a validated antimicrobial drug target. Here, we report the cloning and expression of the P. falciparum enoyl acyl carrier protein reductase gene, which encodes a 50-kDa protein (PfENR) predicted to target to the unique parasite apicoplast. Purified PfENR was crystallized, and its structure resolved as a binary complex with NADH, a ternary complex with triclosan and NAD(+), and as ternary complexes bound to the triclosan analogs 1 and 2 with NADH. Novel structural features were identified in the PfENR binding loop region that most closely. . . homologs; elsewhere the protein was similar to ENR from the plant Brassica napus (root mean square for Cα, 0.30 A). Triclosan and its analogs 1 and 2 killed multidrug-resistant strains of intra-erythrocytic P. falciparum

parasites at sub to low micromolar concentrations in vitro. These data define the structural basis of triclosan binding to PfENR and will facilitate structure-based optimization of PfENR inhibitors.

CT Medical Descriptors:
antiprotozoal activity
apicoplast
article
binding site
Brassica
catalysis
crystallization
drug specificity
drug structure
drug targeting
fatty acid synthesis
gene expression
*malaria
molecular cloning
multidrug resistance
nonhuman
*Plasmodium falciparum
priority journal
protein binding
sequence homology
4 chloro 2 hydroxyphenyl 6' hydroxynaphthyl ether: AN, drug analysis
4 chloro 2 hydroxyphenyl 6' hydroxynaphthyl ether: DV, drug development
*acyl carrier protein
*antiinfective agent: AN, drug analysis
chloroquine
cycloguanil
drug derivative: AN, drug analysis
drug derivative: DV, drug development
fatty acid
n (2,4 dichlorophenyl) 2' hydroxyaniline: AN, drug analysis
n (2,4 dichlorophenyl) 2' hydroxyaniline: DV, drug development
nicotinamide adenine dinucleotide
*oxidoreductase
oxidoreductase inhibitor: AN, drug analysis
oxidoreductase inhibitor: DV, drug development
pyrimethamine
quinine
reduced nicotinamide adenine dinucleotide
sulfadoxine
*triclosan: AN, drug analysis
unclassified drug

RN (chloroquine) 132-73-0, 3545-67-3, 50-63-5, 54-05-7; (cycloguanil) 516-21-2; (nicotinamide adenine dinucleotide) 53-84-9; (oxidoreductase) 9035-73-8, 9035-82-9, 9037-80-3, 9055-15-6; (pyrimethamine) 53640-38-3, 58-14-0; (quinine) 130-89-2, 130-95-0, 14358-44-2, 549-48-4, 549-49-5, 60-93-5, 7549-43-1; (reduced nicotinamide adenine dinucleotide) 58-68-4; (sulfadoxine) 2447-57-6; (triclosan) 3380-34-5

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ACCESSION NUMBER: 2001064519 EMBASE
TITLE: Triclosan offers protection against blood stages of malaria by inhibiting enoyl-ACP reductase of Plasmodium falciparum.
AUTHOR: Surolia, N. (correspondence); Surolia, A.

09763499

CORPORATE SOURCE: Molecular Biology and Genetics Unit, Jawaharlal Nehru Ctr. Adv. Sci. Res., Jakkur, Bangalore, India. surolia@jncasr.ac.in
SOURCE: Nature Medicine, (2001) Vol. 7, No. 2, pp. 167-173.
Refs: 40
ISSN: 1078-8956 CODEN: NAMEFI
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 037 Drug Literature Index
004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Mar 2001
Last Updated on STN: 1 Mar 2001

TI Triclosan offers protection against blood stages of malaria by inhibiting enoyl-ACP reductase of Plasmodium falciparum.

AB The antimicrobial biocide triclosan [5-chloro-2-(2,4-dichlorophenoxy)phenol] potently inhibits the growth of Plasmodium falciparum in vitro and, in a mouse model, Plasmodium berghei in vivo. Inhibition of [(14)C]acetate and [(14)C]malonyl-CoA incorporation into fatty acids in vivo and in vitro, respectively, by triclosan implicate FabI as its target. Here we demonstrate that the enoyl-ACP reductase purified from P. falciparum is triclosan sensitive. Also, we present the evidence for the existence of FabI gene in P. falciparum. We establish the existence of the de novo fatty acid biosynthetic pathway in this parasite, and identify a key enzyme of this pathway for the development of new antimalarials.

CT Medical Descriptors:
amino acid sequence
animal cell
animal model
animal tissue
article
controlled study
drug mechanism
drug potency
drug protein binding
enzyme inhibition
fatty acid synthesis
growth inhibition
life cycle
*malaria: PC, prevention
mouse
nonhuman
*Plasmodium berghei
*Plasmodium falciparum
priority journal
acetic acid
*acyl carrier protein: EC, endogenous compound
*antimalarial agent: CM, drug comparison
*antimalarial agent: DV, drug development
*antimalarial agent: PD, pharmacology
carbon 14
cerulenin: CM, drug comparison
cerulenin: PD, pharmacology
chloroquine: CM, drug comparison
chloroquine: PD, pharmacology

*enoyl acyl carrier protein reductase: EC, endogenous compound
malonyl coenzyme A
nicotinamide adenine dinucleotide: EC, endogenous compound
reduced nicotinamide adenine dinucleotide: EC, endogenous compound
reduced nicotinamide adenine dinucleotide phosphate: EC, endogenous compound
*triclosan: CM, drug comparison
*triclosan: DV, drug development
*triclosan: PD, pharmacology
unclassified drug

RN (acetic acid) 127-08-2, 127-09-3, 64-19-7, 71-50-1; (carbon 14) 14762-75-5; (cerulenin) 17397-89-6; (chloroquine) 132-73-0, 3545-67-3, 50-63-5, 54-05-7; (malonyl coenzyme A) 524-14-1; (nicotinamide adenine dinucleotide) 53-84-9; (reduced nicotinamide adenine dinucleotide phosphate) 53-57-6; (reduced nicotinamide adenine dinucleotide) 58-68-4; (triclosan) 3380-34-5

L15 ANSWER 11 OF 11 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001064504 EMBASE
TITLE: New agents to combat malaria.
AUTHOR: Beeson, J.G. (correspondence); Winstanley, P.A.; McFadden, G.I.; Brown, G.V.
CORPORATE SOURCE: Department of Medicine, University of Melbourne, Royal Melbourne Hospital, Victoria, Australia. beeson@unimelb.edu.au
SOURCE: Nature Medicine, (2001) Vol. 7, No. 2, pp. 149-150.
Refs: 9
ISSN: 1078-8956 CODEN: NAMEFI
COUNTRY: United States
DOCUMENT TYPE: Journal; (Short Survey)
FILE SEGMENT: 030 Clinical and Experimental Pharmacology
036 Health Policy, Economics and Management
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Mar 2001
Last Updated on STN: 1 Mar 2001

TI New agents to combat malaria.

AB Triclosan, an antibacterial agent found in mouthwashes, acne medicines and deodorants, also prevents the growth of Plasmodium falciparum. If properly developed, this type II fatty acid biosynthesis inhibitor may be a promising new antimalarial agent.

CT Medical Descriptors:
antibacterial activity
drug cost
drug efficacy
drug mechanism
human
human cell
human tissue
*malaria: DM, disease management
*malaria: DR, drug resistance
*malaria: DT, drug therapy
Plasmodium falciparum
priority journal
short survey
*antimalarial agent: CM, drug comparison
*antimalarial agent: DV, drug development

*antimalarial agent: DT, drug therapy
*antimalarial agent: PE, pharmacoeconomics
*antimalarial agent: PD, pharmacology
artemether: DT, drug therapy
artemether: PD, pharmacology
atovaquone: DT, drug therapy
atovaquone: PD, pharmacology
benflumetol: DT, drug therapy
benflumetol: PD, pharmacology
chloroquine: DT, drug therapy
chloroquine: PD, pharmacology
fansidar: DT, drug therapy
fansidar: PD, pharmacology
*fatty acid synthesis inhibitor
halofantrine: DT, drug therapy
halofantrine: PD, pharmacology
mefloquine: DT, drug therapy
mefloquine: PD, pharmacology
proguanil: DT, drug therapy
proguanil: PD, pharmacology
quinine: DT, drug therapy
quinine: PD, pharmacology
*thiolactomycin: PD, pharmacology
*triclosan: CM, drug comparison
*triclosan: DV, drug development
*triclosan: DT, drug therapy
*triclosan: PE, pharmacoeconomics
*triclosan: PD, pharmacology
unclassified drug
RN (artemether) 71963-77-4; (atovaquone) 94015-53-9, 95233-18-4; (benflumetol) 82186-77-4; (chloroquine) 132-73-0, 3545-67-3, 50-63-5, 54-05-7; (fansidar) 37338-39-9; (halofantrine) 36167-63-2, 66051-63-6, 66051-74-9, 66051-76-1, 69756-53-2; (mefloquine) 51773-92-3, 53230-10-7; (proguanil) 500-92-5, 637-32-1; (quinine) 130-89-2, 130-95-0, 14358-44-2, 549-48-4, 549-49-5, 60-93-5, 7549-43-1; (thiolactomycin) 82079-32-1; (triclosan) 3380-34-5

=> d his

(FILE 'HOME' ENTERED AT 12:12:49 ON 20 SEP 2008)

FILE 'REGISTRY' ENTERED AT 12:13:14 ON 20 SEP 2008
L1 5 S TRICLOSAN

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CAPLUS, DDFB, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ESBIOBASE, IFIPAT, IMSDRUGNEWS, IMSPRODUCT, IPA, KOSMET, LIFESCI, MEDLINE, NAPRALERT, NLDB, NUTRACEUT, PASCAL, PCTGEN, PHARMAML, ...' ENTERED AT 12:14:55 ON 20 SEP 2008
L2 13207 S L1
L3 19219 S TRICLOSAN
L4 21003 S L2 OR L3
L5 357840 S MALARIA?
L6 124642 S ANTIMALARIA?
L7 408372 S L5 OR L6
L8 474 S L4 AND L7
L9 207454 S FALCIPARUM OR BERGHEI
L10 312 S L8 AND L9
L11 6149 S TRICLOSAN/AB

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L12         166 S L10 AND L11
L13      217939 S QUININE OR ATABRINE OR CHLOROQUINE OR MEFLOQUINE OR PRIMAQUIN
L14          22 S L12 AND L13
L15          11 DUP REM L14 (11 DUPLICATES REMOVED)

=> s l12 and pd<19990623
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'19990623' NOT A VALID FIELD CODE
'19990623' NOT A VALID FIELD CODE
'19990623' NOT A VALID FIELD CODE
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L16           0 L12 AND PD<19990623

=> s l8 and PD<1999
'1999' NOT A VALID FIELD CODE
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'1999' NOT A VALID FIELD CODE
'1999' NOT A VALID FIELD CODE
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'1999' NOT A VALID FIELD CODE
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L17          15 L8 AND PD<1999

=> dup rem
ENTER L# LIST OR (END):l17
DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DGENE, DRUGMONOG2,
IMSPRODUCT, KOSMET, NUTRACEUT, PCTGEN, PHARMAML, USGENE'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L17
L18          14 DUP REM L17 (1 DUPLICATE REMOVED)

=> d l18 1-14 ibib, kwic

L18  ANSWER 1 OF 14  USPATFULL on STN
ACCESSION NUMBER:       1998:82359  USPATFULL
TITLE:                  Enhanced skin penetration system for improved topical
                        delivery of drugs
INVENTOR(S):            Deckner, George Endel, Trumbull, CT, United States
                        Lombardo, Brian Scott, Ansonia, CT, United States
PATENT ASSIGNEE(S):     Richardson-Vicks Inc., Shelton, CT, United States (U.S.
                        corporation)

                             NUMBER       KIND    DATE
                        ---------------- ------ --------
PATENT INFORMATION:     US 5780049               19980714           <--
APPLICATION INFO.:      US 1995-464991           19950605  (8)
RELATED APPLN. INFO.:   Division of Ser. No. US 1995-390902, filed on 16 Feb
                        1995, now abandoned which is a continuation of Ser. No.
                        US 1994-228167, filed on 15 Apr 1994, now abandoned
```

which is a continuation of Ser. No. US 1993-111032, filed on 24 Aug 1993, now abandoned which is a continuation of Ser. No. US 1992-957752, filed on 2 Oct 1992, now abandoned which is a continuation of Ser. No. US 1991-778424, filed on 16 Oct 1991, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rose, Shep K.
LEGAL REPRESENTATIVE: Henderson, Loretta J., Dabbiere, David K.
NUMBER OF CLAIMS: 13
EXEMPLARY CLAIM: 1
LINE COUNT: 698
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . as retinoic acid and its derivatives (e.g., cis and trans); antibiotics and antimicrobials such as benzoyl peroxide, octopirox, erythromycin, tetracyclin, triclosan, azelaic acid and its derivatives, phenoxy ethanol and phenoxy proponol, ethylacetate, clindamycin and meclocycline; sebostats such as flavinoids; hydroxy acids;. . .

SUMM . . . inclusion in compositions of the present invention include pharmaceutically-acceptable salts of β-lactam drugs, quinolone drugs, ciprofloxacin, norfloxacin, tetracycline, erythromycin, amikacin, triclosan, doxycycline, capreomycin, chlorhexidine, chlortetracycline, oxytetracycline, clindamycin, ethambutol, metronidazole, pentamidine, gentamicin, kanamycin, lineomycin, methacycline, methenamine, minocycline, neomycin, netilmicin, paromomycin, streptomycin, tobramycin,. . . methenamine mandelate, minocycline hydrochloride, neomycin sulfate, netilmicin sulfate, paromomycin sulfate, streptomycin sulfate, tobramycin sulfate, miconazole hydrochloride, amanfadine hydrochloride, amanfadine sulfate, triclosan, octopirox, parachlorometa xylenol, nystatin, tolnaftate and clotrimazole.

SUMM Useful drug actives in the compositions of the present invention include antimalarial drugs. Antimalarial drugs preferred for inclusion in compositions of the present invention include pharmaceutically-acceptable salts of chloroquine, hydroxychloroquine primaquine and quinine.

CLM What is claimed is:

. . . of an antimicrobial pharmaceutical active selected from the group consisting of β-lactam drugs, quinolone drugs, ciprofloxacin, norfloxacin, tetracycline, erythromycin, amikacin, triclosan, doxycycline, capremycin, chlorhexidine, chlortetracycline, oxytetracycline, clindamycin, ethambutol, metronidazole, pentamidine, gentamicin, kanamycin, lineomycin, methacycline, methenamine, minocycline, neomycin, netilmicin, paromomycin, streptomycin, tobramycin, miconazole, amanfadine, triclosan, octopirox, parachlorometa xylenol, nystatin, tolnaftate, clotrimazole, pharmaeutically-acceptable salts thereof, and mixtures thereof; and (c) from about 0.05% to about 5%. . .

CLM What is claimed is:

. . . said antimicrobial pharmaceutical active is selected from the group consisting of β-lactam drugs, quinolone drugs, ciprofloxacin, norfloxacin, tetracycline, erythromycin, amikacin, triclosan, doxycycline, capremycin, chlorhexidine, chlortetracycline, oxytetracycline, clindamycin, ethambutol, metronidazole, pentamidine, gentamicin, kanamycin, lineomycin, methacycline, methenamine, minocycline, neomycin, netilmicin, paromomycin, streptomycin, tobramycin,. . .

CLM What is claimed is:

. . . methenamine mandelate, minocycline hydrochloride, neomycin sulfate, netilmicin sulfate, paromomycin sulfate, streptomycin sulfate, tobramycin sulfate, miconazole hydrochloride, amanfadine hydrochloride, amanfadine sulfate, triclosan, octopirox, parachlorometa xylenol, nystatin, tolnaftate and clotrimazole.

IT 55-56-1, Chlorhexidine 57-62-5, Chlortetracycline 57-92-1, Streptomycin, biological studies 59-01-8, Kanamycin 74-55-5, Ethambutol 79-57-2, Oxytetracycline 100-33-4, Pentamidine 100-97-0, biological studies 154-21-2 443-48-1, Metronidazole 564-25-0 768-94-5, Tricyclo[3.3.1.13,7]decan-1-amine 914-00-1, Methacycline 1403-66-3, Gentamicin 1404-04-2, Neomycin 3380-34-5, Triclosan 7542-37-2, Paromomycin 10118-90-8, Minocycline 11003-38-6, Capreomycin 22916-47-8, Miconazole 32986-56-4, Tobramycin 37517-28-5, Amikacin 56391-56-1, Netilmicin 70458-96-7, Norfloxacin 85721-33-1, Ciprofloxacin
(antimicrobial topical compns. containing polyacrylamide and)

L18 ANSWER 2 OF 14 USPATFULL on STN
ACCESSION NUMBER: 1998:78738 USPATFULL
TITLE: Enhanced skin penetration system for improved topical delivery of drugs
INVENTOR(S): Deckner, George Endel, Trumbull, CT, United States
Lombardo, Brian Scott, Ansonia, CT, United States
PATENT ASSIGNEE(S): Richardson-Vicks Inc., Shelton, CT, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5776485		19980707	<--
APPLICATION INFO.:	US 1995-469701		19950606	(8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1995-390902, filed on 16 Feb 1995, now abandoned which is a continuation of Ser. No. US 1994-228167, filed on 15 Apr 1994, now abandoned which is a continuation of Ser. No. US 1993-111032, filed on 24 Aug 1993, now abandoned which is a continuation of Ser. No. US 1992-957752, filed on 2 Oct 1992, now abandoned which is a continuation of Ser. No. US 1991-778424, filed on 16 Oct 1991, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rose, Shep K.
LEGAL REPRESENTATIVE: Henderson, Loretta J., Dabbiere, David K.
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
LINE COUNT: 700
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . as retinoic acid and its derivatives (e.g., cis and trans); antibiotics and antimicrobials such as benzoyl peroxide, octopirox, erythromycin, tetracyclin, triclosan, azelaic acid and its derivatives, phenoxy ethanol and phenoxy proponol, ethylacetate, clindamycin and meclocycline; sebostats such as flavinoids; hydroxy acids;. . .

SUMM . . . inclusion in compositions of the present invention include pharmaceutically-acceptable salts of β-lactam drugs, quinolone drugs, ciprofloxacin, norfloxacin, tetracycline, erythromycin, amikacin, triclosan, doxycycline, capreomycin, chlorhexidine, chlortetracycline, oxytetracycline, clindamycin, ethambutol, metronidazole, pentamidine, gentamicin, kanamycin, lineomycin,

methacycline, methenamine, minocycline, neomycin, netilmicin, paromomycin, streptomycin, tobramycin,. . . methenamine mandelate, minocycline hydrochloride, neomycin sulfate, netilmicin sulfate, paromomycin sulfate, streptomycin sulfate, tobramycin sulfate, miconazole hydrochloride, amanfadine hydrochloride, amanfadine sulfate, triclosan, octopirox, parachlorometa xylenol, nystatin, tolnaftate and clotrimazole.

SUMM Useful drug actives in the compositions of the present invention include antimalarial drugs. Antimalarial drugs preferred for inclusion in compositions of the present invention include pharmaceutically-acceptable salts of chloroquine, hydroxychloroquine primaquine and quinine.

IT 55-56-1, Chlorhexidine 57-62-5, Chlortetracycline 57-92-1, Streptomycin, biological studies 59-01-8, Kanamycin 74-55-5, Ethambutol 79-57-2, Oxytetracycline 100-33-4, Pentamidine 100-97-0, biological studies 154-21-2 443-48-1, Metronidazole 564-25-0 768-94-5, Tricyclo[3.3.1.13,7]decan-1-amine 914-00-1, Methacycline 1403-66-3, Gentamicin 1404-04-2, Neomycin 3380-34-5, Triclosan 7542-37-2, Paromomycin 10118-90-8, Minocycline 11003-38-6, Capreomycin 22916-47-8, Miconazole 32986-56-4, Tobramycin 37517-28-5, Amikacin 56391-56-1, Netilmicin 70458-96-7, Norfloxacin 85721-33-1, Ciprofloxacin
(antimicrobial topical compns. containing polyacrylamide and)

L18 ANSWER 3 OF 14 USPATFULL on STN

ACCESSION NUMBER:	1998:75176 USPATFULL
TITLE:	Enhanced skin penetration system for improving topical delivery of drugs
INVENTOR(S):	Deckner, George Endel, Trumbull, CT, United States Lombardo, Brian Scott, Ansonia, CT, United States
PATENT ASSIGNEE(S):	Richardson-Vicks Inc., Shelton, CT, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5773023		19980630	<--
APPLICATION INFO.:	US 1995-462710		19950605	(8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1995-390902, filed on 16 Feb 1995, now abandoned which is a continuation of Ser. No. US 1994-228167, filed on 15 Apr 1994, now abandoned which is a continuation of Ser. No. US 1993-111032, filed on 24 Aug 1993, now abandoned which is a continuation of Ser. No. US 1992-957752, filed on 2 Oct 1992, now abandoned which is a continuation of Ser. No. US 1991-778424, filed on 16 Oct 1991, now abandoned			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Rose, Shep K.			
LEGAL REPRESENTATIVE:	Henderson, Loretta J., Dabbiere, David K.			
NUMBER OF CLAIMS:	29			
EXEMPLARY CLAIM:	1			
LINE COUNT:	745			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . as retinoic acid and its derivatives (e.g., cis and trans); antibiotics and antimicrobials such as benzoyl peroxide, octopirox, erythromycin, tetracyclin, triclosan, azelaic acid and its derivatives, phenoxy ethanol and phenoxy proponol, ethylacetate, clindamycin and meclocycline; sebostats such as flavinoids; hydroxy acids;. . .

SUMM . . . inclusion in compositions of the present invention include pharmaceutically-acceptable salts of β-lactam drugs, quinolone drugs, ciprofloxacin, norfloxacin, tetracycline, erythromycin, amikacin, triclosan, doxycycline, capreomycin, chlorhexidine, chlortetracycline, oxytetracycline, clindamycin, ethambutol, metronidazole, pentamidine, gentamicin, kanamycin, lineomycin, methacycline, methenamine, minocycline, neomycin, netilmicin, paromomycin, streptomycin, tobramycin,. . . methenamine mandelate, minocycline hydrochloride, neomycin sulfate, netilmicin sulfate, paromomycin sulfate, streptomycin sulfate, tobramycin sulfate, miconazole hydrochloride, amanfadine hydrochloride, amanfadine sulfate, triclosan, octopirox, parachlorometa xylenol, nystatin, tolnaftate and clotrimazole.

SUMM Useful drug actives in the compositions of the present invention include antimalarial drugs. Antimalarial drugs preferred for inclusion in compositions of the present invention include pharmaceutically-acceptable salts of chloroquine, hydroxychloroquine primaquine and quinine.

CLM What is claimed is:

. . . diuretic drugs, vasodilator drugs, vasoconstrictor drugs, anti-ulcer drugs, anesthetic drugs, antidepressant drugs, tranquilizer and sedative drugs, antipsychotic drugs, antineoplastic drugs, antimalarial drugs, muscle relaxant drugs, antispasmodic drugs, antidiarrlieal drugs, bone-active drugs and mixtures thereof; and (c) from about 0.05% to about. . .

IT 55-56-1, Chlorhexidine 57-62-5, Chlortetracycline 57-92-1, Streptomycin, biological studies 59-01-8, Kanamycin 74-55-5, Ethambutol 79-57-2, Oxytetracycline 100-33-4, Pentamidine 100-97-0, biological studies 154-21-2 443-48-1, Metronidazole 564-25-0 768-94-5, Tricyclo[3.3.1.13,7]decan-1-amine 914-00-1, Methacycline 1403-66-3, Gentamicin 1404-04-2, Neomycin 3380-34-5, Triclosan 7542-37-2, Paromomycin 10118-90-8, Minocycline 11003-38-6, Capreomycin 22916-47-8, Miconazole 32986-56-4, Tobramycin 37517-28-5, Amikacin 56391-56-1, Netilmicin 70458-96-7, Norfloxacin 85721-33-1, Ciprofloxacin
(antimicrobial topical compns. containing polyacrylamide and)

L18 ANSWER 4 OF 14 USPATFULL on STN

ACCESSION NUMBER:	1998:57546 USPATFULL
TITLE:	Enhanced skin penetration system for improved topical delivery of drugs
INVENTOR(S):	Deckner, George Endel, Trumbull, CT, United States Lombardo, Brian Scott, Ansonia, CT, United States
PATENT ASSIGNEE(S):	Richardson-Vicks Inc., Shelton, CT, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5756119		19980526	<--
APPLICATION INFO.:	US 1995-462376		19950605 (8)	
RELATED APPLN. INFO.:	Division of Ser. No. US 1995-390902, filed on 16 Feb 1995, now abandoned which is a continuation of Ser. No. US 1994-228167, filed on 15 Apr 1994, now abandoned which is a continuation of Ser. No. US 1993-111032, filed on 24 Aug 1993, now abandoned which is a continuation of Ser. No. US 1992-957752, filed on 2 Oct 1992, now abandoned which is a continuation of Ser. No. US 1991-778424, filed on 16 Oct 1991, now abandoned			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			

PRIMARY EXAMINER: Rose, Shep K.
LEGAL REPRESENTATIVE: Henderson, Loretta J., Dabbiere, David K.
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
LINE COUNT: 697
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . as retinoic acid and its derivatives (e.g., cis and trans); antibiotics and antimicrobials such as benzoyl peroxide, octopirox, erythromycin, tetracylin, triclosan, azelaic acid and its derivatives, phenoxy ethanol and phenoxy proponol, ethylacetate, clindamycin and meclocycline; sebostats such as flavinoids; hydroxy acids;. . .

SUMM . . . inclusion in compositions of the present invention include pharmaceutically-acceptable salts of β-lactam drugs, quinolone drugs, ciprofloxacin, norfloxacin, tetracycline, erythromycin, amikacin, triclosan, doxycycline, capreomycin, chlorhexidine, chlortetracycline, oxytetracycline, clindamycin, ethambutol, metronidazole, pentamidine, gentamicin, kanamycin, lineomycin, methacycline, methenamine, minocycline, neomycin, netilmicin, paromomycin, streptomycin, tobramycin,. . . methenamine mandelate, minocycline hydrochloride, neomycin sulfate, netilmicin sulfate, paromomycin sulfate, streptomycin sulfate, tobramycin sulfate, miconazole hydrochloride, amanfadine hydrochloride, amanfadine sulfate, triclosan, octopirox, parachlorometa xylenol, nystatin, tolnaftate and clotrimazole.

SUMM Useful drug actives in the compositions of the present invention include antimalarial drugs. Antimalarial drugs preferred for inclusion in compositions of the present invention include pharmaceutically-acceptable salts of chloroquine, hydroxychloroquine primaquine and quinine.

IT 55-56-1, Chlorhexidine 57-62-5, Chlortetracycline 57-92-1, Streptomycin, biological studies 59-01-8, Kanamycin 74-55-5, Ethambutol 79-57-2, Oxytetracycline 100-33-4, Pentamidine 100-97-0, biological studies 154-21-2 443-48-1, Metronidazole 564-25-0 768-94-5, Tricyclo[3.3.1.13,7]decan-1-amine 914-00-1, Methacycline 1403-66-3, Gentamicin 1404-04-2, Neomycin 3380-34-5, Triclosan 7542-37-2, Paromomycin 10118-90-8, Minocycline 11003-38-6, Capreomycin 22916-47-8, Miconazole 32986-56-4, Tobramycin 37517-28-5, Amikacin 56391-56-1, Netilmicin 70458-96-7, Norfloxacin 85721-33-1, Ciprofloxacin
(antimicrobial topical compns. containing polyacrylamide and)

L18 ANSWER 5 OF 14 USPATFULL on STN
ACCESSION NUMBER: 1998:57545 USPATFULL
TITLE: Enhanced skin penetration system for improved topical delivery of drugs
INVENTOR(S): Deckner, George Endel, Trumbull, CT, United States
Lombardo, Brian Scott, Ansonia, CT, United States
PATENT ASSIGNEE(S): Richardson-Vicks Inc., Shelton, CT, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5756118		19980526	<--
APPLICATION INFO.:	US 1995-462258		19950605	(8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1995-390902, filed on 16 Feb 1995, now abandoned which is a continuation of Ser. No. US 1994-228167, filed on 15 Apr 1994, now abandoned which is a continuation of Ser. No. US 1993-111032,			

filed on 24 Aug 1993, now abandoned which is a continuation of Ser. No. US 1992-957752, filed on 2 Oct 1992, now abandoned which is a continuation of Ser. No. US 1991-778424, filed on 16 Oct 1991, now abandoned

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rose, Shep K.
LEGAL REPRESENTATIVE: Henderson, Loretta J., Dabbiere, David K.
NUMBER OF CLAIMS: 16
EXEMPLARY CLAIM: 1
LINE COUNT: 682
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . as retinoic acid and its derivatives (e.g., cis and trans); antibiotics and antimicrobials such as benzoyl peroxide, octopirox, erythromycin, tetracyclin, triclosan, azelaic acid and its derivatives, phenoxy ethanol and phenoxy proponol, ethylacetate, clindamycin and meclocycline; sebostats such as flavinoids; hydroxy acids;. . .

SUMM . . . inclusion in compositions of the present invention include pharmaceutically-acceptable salts of β-lactam drugs, quinolone drugs, ciprofloxacin, norfloxacin, tetracycline, erythromycin, amikacin, triclosan, doxycycline, capreomycin, chlorhexidine, chlortetracycline, oxytetracycline, clindamycin, ethambutol, metronidazole, pentamidine, gentamicin, kanamycin, lineomycin, methacycline, methenamine, minocycline, neomycin, netilmicin, paromomycin, streptomycin, tobramycin,. . . methenamine mandelate, minocycline hydrochloride, neomycin sulfate, netilmicin sulfate, paromomycin sulfate, streptomycin sulfate, tobramycin sulfate, miconazole hydrochloride, amanfadine hydrochloride, amanfadine sulfate, triclosan, octopirox, parachlorometa xylenol, nystatin, tolnaftate and clotrimazole.

SUMM Useful drug actives in the compositions of the present invention include antimalarial drugs. Antimalarial drugs preferred for inclusion in compositions of the present invention include pharmaceutically-acceptable salts of chloroquine, hydroxychloroquine primaquine and quinine.

IT 55-56-1, Chlorhexidine 57-62-5, Chlortetracycline 57-92-1, Streptomycin, biological studies 59-01-8, Kanamycin 74-55-5, Ethambutol 79-57-2, Oxytetracycline 100-33-4, Pentamidine 100-97-0, biological studies 154-21-2 443-48-1, Metronidazole 564-25-0 768-94-5, Tricyclo[3.3.1.13,7]decan-1-amine 914-00-1, Methacycline 1403-66-3, Gentamicin 1404-04-2, Neomycin 3380-34-5, Triclosan 7542-37-2, Paromomycin 10118-90-8, Minocycline 11003-38-6, Capreomycin 22916-47-8, Miconazole 32986-56-4, Tobramycin 37517-28-5, Amikacin 56391-56-1, Netilmicin 70458-96-7, Norfloxacin 85721-33-1, Ciprofloxacin
(antimicrobial topical compns. containing polyacrylamide and)

L18 ANSWER 6 OF 14 USPATFULL on STN
ACCESSION NUMBER: 1998:47986 USPATFULL
TITLE: High viscosity liquid controlled delivery system
INVENTOR(S): Tipton, Arthur J., Birmingham, AL, United States
Holl, Richard J., Birmingham, AL, United States
PATENT ASSIGNEE(S): Southern Biosystems, Inc., Birmingham, AL, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5747058		19980505	<--

APPLICATION INFO.: US 1995-474337 19950607 (8)
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Azpuru, Carlos A.
LEGAL REPRESENTATIVE: Kilpatrick Stockton LLP, Meredith, Esq., Roy D.
NUMBER OF CLAIMS: 95
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 17 Drawing Figure(s); 9 Drawing Page(s)
LINE COUNT: 1344
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . and PGF.sub.2 ; antipyretics such as aspirin, sodium salicylate, and salicylamide; antispasmodics such as atropine, methantheline, papaverine, and methscopolamine bromide; antimalarials such as the 4-aminoquinolines, 8-aminoquinolines, chloroquine, and pyrimethamine, antihistamines such as diphenhydramine, dimenhydrinate, tripelennamine, perphenazine, and chlorphenazine; cardioactive agents such. . .

DETD Antimicrobial active agents that are currently used in mouthwash formulations can include, but not limited to, domiphen bromide, triclosan, chlorhexidine, essential oils, cetyl pyridinium chloride, fluorides, alexidine, salicylanilides, zinc compounds, and antibiotics. They can be used either singly or. . .

L18 ANSWER 7 OF 14 USPATFULL on STN
ACCESSION NUMBER: 1998:17360 USPATFULL
TITLE: Compositions and methods for topical administration of pharmaceutically active agents
INVENTOR(S): Kanios, David P., Miami, FL, United States
Gentile, Joseph A., Plantation, FL, United States
Mantelle, Juan A., Miami, FL, United States
Sablotsky, Steven, Miami, FL, United States
PATENT ASSIGNEE(S): Noven Pharmaceuticals, Inc., Miami, FL, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5719197		19980217	<--
APPLICATION INFO.:	US 1995-477361		19950607 (8)	

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-112330, filed on 27 Aug 1993, now patented, Pat. No. US 5446070 which is a continuation-in-part of Ser. No. US 1991-813196, filed on 23 Dec 1991, now patented, Pat. No. US 5234957 which is a continuation-in-part of Ser. No. US 1991-661827, filed on 27 Feb 1991, now abandoned , said Ser. No. US 1995-477361, filed on 7 Jun 1995 which is a continuation-in-part of Ser. No. US 1993-67001, filed on 26 May 1993 which is a continuation of Ser. No. US 1991-671709, filed on 2 Apr 1991, now patented, Pat. No. US 5300291 which is a continuation-in-part of Ser. No. US 1989-295847, filed on 11 Jan 1989, now patented, Pat. No. US 4994267 which is a continuation-in-part of Ser. No. US 1988-164482, filed on 4 Mar 1988, now patented, Pat. No. US 4814168
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Azpuru, Carlos A.
LEGAL REPRESENTATIVE: Foley & Lardner
NUMBER OF CLAIMS: 27
EXEMPLARY CLAIM: 1

LINE COUNT: 1799
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD ANTIMALARIAL such as Acedapsone, Alphaaminoquinolines, 4-Aminoquinolines, Amodiaquin, Arteether, Artemether, Artemisinin, Artesunate, Bebeerine, Berberine, Chirata, Chlorguanide, Chloroquine, Chlorproguanil, Cinchona, Cinchonidine, Cinchonine, Cycloguanil,. . .
DETD . . . as Bornyl Chloride, Calcium Iodate, Iodine, Iodine Monochloride, Iodine Trichloride, Iodoform, Povidone-Iodine, Sodium Hypochlorite, Sodium Iadate, Symclosene, Thymol Iodide, Triclocarban, Triclosan, Troclosene Potassium
CLM What is claimed is:
. . . cholinergic blocking drugs, mydriatics, psychic energizers, humoral agents, antispasmodic drugs, antidepressants, antidiabetics, anorexic drugs, anti-allergic drugs, decongestants, antipyretics, anti-migraine drugs, antimalarial, antiulcer drugs, peptides, and anti-estrogens.

L18 ANSWER 8 OF 14 USPATFULL on STN
ACCESSION NUMBER: 1998:4239 USPATFULL
TITLE: Gel type cosmetic compositions
INVENTOR(S): Deckner, George Endel, Trumbull, CT, United States
Lombardo, Brian Scott, Ansonia, CT, United States
PATENT ASSIGNEE(S): Richardson-Vicks Inc., Shelton, CT, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5707635		19980113	<--
APPLICATION INFO.:	US 1994-249093		19940525 (8)	

RELATED APPLN. INFO.: Continuation of Ser. No. US 1993-121661, filed on 15 Sep 1993, now abandoned which is a continuation of Ser. No. US 1992-931553, filed on 18 Aug 1992, now abandoned which is a continuation of Ser. No. US 1991-778423, filed on 16 Oct 1991, now abandoned
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Hulina, Amy
LEGAL REPRESENTATIVE: Henderson, Loretta J., Dabbiere, David K.
NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
LINE COUNT: 513
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . vasodilator drugs, vasoconstrictor drugs, anti-ulcer drugs, anesthetic drugs, antidepressant drugs, tranquilizer and sedative drugs, antipsychotic drugs, antimicrobial drugs, antineoplastic drugs, antimalarial drugs, muscle relaxant drugs, antispasmodic drugs, antidiarrheal drugs and bone-active drugs and mixtures thereof.
SUMM . . . as retinoic acid and its derivatives (e.g., cis and trans); antibiotics and antimicrobials such as benzoyl peroxide, octopirox, erythromycin, tetracyclin, triclosan, azelaic acid and its derivatives, phenoxy ethanol and phenoxy proponol, ethylacetate, clindamycin and meclocycline; sebostats such as flavinoids; alpha and. . .

L18 ANSWER 9 OF 14 IFIPAT COPYRIGHT 2008 IFI on STN DUPLICATE 1
AN 02825061 IFIPAT;IFIUDB;IFICDB
TITLE: COMPOSITIONS FOR TOPICAL DELIVERY OF DRUGS COMPRISING

	A MIXTURE OF HIGH AND LOW HLB SURFACTANTS AND ALKOXYLATED ETHER; TRANSDERMAL
INVENTOR(S):	Bloom, Roberta C, Huntington, CT Deckner, George E, Cincinnati, OH
PATENT ASSIGNEE(S):	The Procter & Gamble Company, Cincinnati, OH
PRIMARY EXAMINER:	Kulkosky, Peter F
AGENT:	Dabbiere, David K Sabatelli, Anthony D

	NUMBER	PK	DATE
PATENT INFORMATION:	US 5614178	A	19970325
	(CITED IN 027 LATER PATENTS)		
APPLICATION INFORMATION:	US 1994-265975		19940627
EXPIRATION DATE:	25 Mar 2014		

	APPLN. NUMBER	DATE	GRANTED PATENT NO. OR STATUS
CONTINUATION OF:	US 1992-950527	19920925	ABANDONED
CONTINUATION OF:	US 1993-79977	19930625	ABANDONED
CONTINUATION-IN-PART OF:	US 1992-920937	19920728	ABANDONED
CONTINUATION-IN-PART OF:	US 1993-33211	19930318	ABANDONED
FAMILY INFORMATION:	US 5614178	19970325	
DOCUMENT TYPE:	Utility Certificate of Correction		
CORRECTION DATE:	29 Jul 1997		
FILE SEGMENT:	CHEMICAL GRANTED		
ENTRY DATE:	Entered STN: 28 Mar 1997 Last Updated on STN: 6 Nov 1997		

MICROFILM REEL NO:	008118 FRAME NO: 0921
NUMBER OF CLAIMS:	45

PI US 5614178 A 19970325 (CITED IN 027 LATER PATENTS)

ACLM . . . vasodilator drugs, vasoconstrictor drugs, anti-ulcer drugs, anesthetic drugs, antidepressant drugs, tranquilizer and sedative drugs, antipsychotic drugs, antimicrobial drugs, antineoplastic drugs, antimalarial drugs, muscle relaxant drugs, antispasmodic drugs, antidiarrheal drugs and bone-active drugs and mixtures thereof.

. . . drug is selected from the group consisting of Beta -lactam drugs, quinolone drugs, ciprofloxacin, norfloxacin, tetracycline, erythromycin, hexamidine isethionate, amikacin, triclosan, doxycycline, capreomycin, chlorhexidine, chlortetracycline, oxytetracycline, clindamycin, ethambutol, metronidazole, pentamidine, gentamicin, kanamycin, lineomycin, methacycline, methenamine, minocycline, neomycin, netilmicin, paromomycin, streptomycin, tobramycin, . . .

. . . vasodilator drugs, vasoconstrictor drugs, anti-ulcer drugs, anesthetic drugs, antidepressant drugs, tranquilizer and sedative drugs, antipsychotic drugs, antimicrobial drugs, antineoplastic drugs, antimalarial drugs, muscle relaxant drugs, antispasmodic drugs, antidiarrheal drugs and bone-active drugs and mixtures thereof.

L18 ANSWER 10 OF 14 USPATFULL on STN

ACCESSION NUMBER:	97:70731 USPATFULL
TITLE:	Solubility parameter based drug delivery system and method for altering drug saturation concentration
INVENTOR(S):	Miranda, Jesus, Miami, FL, United States Sablotsky, Steven, Miami, FL, United States
PATENT ASSIGNEE(S):	Noven Pharmaceuticals, Inc., Miami, FL, United States

(U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5656286		19970812	<--
APPLICATION INFO.:	US 1994-178558		19940107	(8)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1991-722342, filed on 27 Jun 1991, now patented, Pat. No. US 5474783 which is a continuation-in-part of Ser. No. US 1991-671709, filed on 2 Apr 1991, now patented, Pat. No. US 5300291 which is a continuation-in-part of Ser. No. US 1989-295847, filed on 11 Jan 1989, now patented, Pat. No. US 4994267, issued on 19 Feb 1991 which is a continuation-in-part of Ser. No. US 1988-164482, filed on 4 Mar 1988, now patented, Pat. No. US 4814168, issued on 21 Mar 1989			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Venkat, Jyothsna			
LEGAL REPRESENTATIVE:	Foley & Lardner			
NUMBER OF CLAIMS:	73			
EXEMPLARY CLAIM:	1,4			
NUMBER OF DRAWINGS:	20 Drawing Figure(s); 19 Drawing Page(s)			
LINE COUNT:	3344			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD 48. Antimalarial drugs such as Acedapsone, Amodiaquin, Arteether, Artemether, Artemisinin, Artesunate, Bebeerine, Berberine, Chirata, Chlorguanide, Chloroquine, Chlorproguanil, Cinchona, Cinchonidine, Cinchonine, Cycloguanil, Gentiopicrin,. . .

DETD . . . Iodic Acid, Iodine, Iodine Monochloride, Iodine Trichloride, Iodoform, Methenamine Tetraiodine, Oxychlorosene, Povidone-Iodine, Sodium Hypochlorite, Sodium Iodate, Symclosene, Thymol Iodide, Triclocarban, Triclosan and Troclosene Potassium;

L18 ANSWER 11 OF 14 USPATFULL on STN

ACCESSION NUMBER:	95:78209 USPATFULL
TITLE:	Compositions and methods for topical administration of pharmaceutically active agents
INVENTOR(S):	Mantelle, Juan A., Miami, FL, United States
PATENT ASSIGNEE(S):	Nover Pharmaceuticals, Inc., Miami, FL, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5446070		19950829	<--
APPLICATION INFO.:	US 1993-112330		19930827	(8)
DISCLAIMER DATE:	20100810			
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1991-813196, filed on 23 Dec 1991, now patented, Pat. No. US 5234957 which is a continuation-in-part of Ser. No. US 1991-661827, filed on 27 Feb 1991, now abandoned			
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Page, Thurman K.			
ASSISTANT EXAMINER:	Azpuru, Carlos			
LEGAL REPRESENTATIVE:	Foley & Lardner			
NUMBER OF CLAIMS:	45			
EXEMPLARY CLAIM:	1			
LINE COUNT:	2434			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD ANTIMALARIAL such as Acedapsone, Alphaaminoquinolines, 4-Aminoquinolines, Amodiaquin, Arteether, Artemether, Artemisinin, Artesunate, Bebeerine, Berberine, Chirata, Chlorguanide, Chloroquine, Chlorproguanil, Cinchona, Cinchonidine, Cinchonine, Cycloguanil,. . .

DETD . . . such as Bornyl Chloride, Calcium Iodate, Iodine,Iodine Monochloride, Iodine Trichloride, Iodoform, Povidone-Iodine, Sodium Hypochlorite, Sodium Iodate, Symclosene, Thymol Iodide, Triclocarban, Triclosan, Troclosene Potassium

CLM What is claimed is:

. . . cholinergic blocking drugs, mydriatics, psychic energizers, humoral agents, antispasmodic drugs, antidepressants, antidiabetics, anorexic drugs, anti-allergic drugs, decongestants, antipyretics, antimigraine drugs, antimalarial, antiulcer drugs, peptides, and anti-estrogens.

L18 ANSWER 12 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:503333 CAPLUS
DOCUMENT NUMBER: 119:103333
ORIGINAL REFERENCE NO.: 119:18441a,18444a
TITLE: Enhanced skin penetration system for improved topical delivery of drugs
INVENTOR(S): Deckner, George Endel; Lombardo, Brian Scott
PATENT ASSIGNEE(S): Richardson-Vicks, Inc., USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9307903	A1	19930429	WO 1992-US8744	19921013 <--
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9228639	A	19930521	AU 1992-28639	19921013 <--
AU 675212	B2	19970130		
EP 608322	A1	19940803	EP 1992-921769	19921013 <--
EP 608322	B1	19980722		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
JP 07500594	T	19950119	JP 1993-507771	19921013 <--
JP 3471354	B2	20031202		
HU 67046	A2	19950130	HU 1994-1106	19921013 <--
BR 9206631	A	19951024	BR 1992-6631	19921013 <--
AT 168563	T	19980815	AT 1992-921769	19921013 <--
ES 2118834	T3	19981001	ES 1992-921769	19921013 <--
CA 2117265	C	20000801	CA 1992-2117265	19921013
CN 1072602	A	19930602	CN 1992-113328	19921016 <--
CN 1050763	C	20000329		
US 6277892	B1	20010821	US 1994-191734	19940204
NO 9401317	A	19940616	NO 1994-1317	19940413 <--
FI 9401770	A	19940415	FI 1994-1770	19940415 <--
HK 1013002	A1	20000623	HK 1998-114300	19981221
PRIORITY APPLN. INFO.:			US 1991-778422 A	19911016
			US 1992-948391 A	19920925

				WO 1992-US8744	A 19921013
				US 1993-59001	B1 19930506
PI	WO 9307903 A1 19930429				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9307903	A1	19930429	WO 1992-US8744	19921013 <--
	W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
	AU 9228639	A	19930521	AU 1992-28639	19921013 <--
	AU 675212	B2	19970130		
	EP 608322	A1	19940803	EP 1992-921769	19921013 <--
	EP 608322	B1	19980722		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
	JP 07500594	T	19950119	JP 1993-507771	19921013 <--
	JP 3471354	B2	20031202		
	HU 67046	A2	19950130	HU 1994-1106	19921013 <--
	BR 9206631	A	19951024	BR 1992-6631	19921013 <--
	AT 168563	T	19980815	AT 1992-921769	19921013 <--
	ES 2118834	T3	19981001	ES 1992-921769	19921013 <--
	CA 2117265	C	20000801	CA 1992-2117265	19921013
	CN 1072602	A	19930602	CN 1992-113328	19921016 <--
	CN 1050763	C	20000329		
	US 6277892	B1	20010821	US 1994-191734	19940204
	NO 9401317	A	19940616	NO 1994-1317	19940413 <--
	FI 9401770	A	19940415	FI 1994-1770	19940415 <--
	HK 1013002	A1	20000623	HK 1998-114300	19981221

IT Anesthetics
Anti-infective agents
Antiarrhythmics
Antidepressants
Antiemetics
Antihistaminics
Antihypertensives
Antimalarials
Antitussives
Appetite depressants
Cardiotonics
Cholinergic agonists
Diuretics
Hypnotics and Sedatives
Inflammation inhibitors
Muscle relaxants
Neoplasm inhibitors
Nervous system stimulants
Sunscreens
Tranquilizers and Neuroleptics
Ulcer inhibitors
Vasoconstrictors
Vasodilators
Wound healing promoters
(topical compns. containing dialkylaminoalkyl acrylate polymers and)

IT 55-56-1, Chlorhexidine 57-62-5, Chlortetracycline 57-92-1, Streptomycin, biological studies 59-01-8, Kanamycin 74-55-5, Ethambutol 79-57-2, Oxytetracycline 100-33-4, Pentamidine 100-97-0, biological studies 154-21-2 443-48-1, Metronidazole 564-25-0 768-94-5, Tricyclo[3.3.1.13,7]decan-1-amine 914-00-1, Methacycline 1403-66-3, Gentamicin 1404-04-2, Neomycin 3380-34-5, Triclosan 7542-37-2, Paromomycin 10118-90-8, Minocycline

11003-38-6, Capreomycin 22916-47-8, Miconazole 32986-56-4, Tobramycin
37517-28-5, Amikacin 56391-56-1, Netilmicin 70458-96-7, Norfloxacin
85721-33-1, Ciprofloxacin
RL: BIOL (Biological study)
(antimicrobial topical compns. containing dialkylaminoalkyl acrylate
polymers and)

L18 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:503334 CAPLUS
DOCUMENT NUMBER: 119:103334
ORIGINAL REFERENCE NO.: 119:18441a,18444a
TITLE: Enhanced skin penetration system for improved topical delivery of drugs
INVENTOR(S): Deckner, George Endel; Lombardo, Brian Scott
PATENT ASSIGNEE(S): Richardson-Vicks, Inc., USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9307902	A1	19930429	WO 1992-US8741	19921013 <--
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9228064	A	19930521	AU 1992-28064	19921013 <--
AU 675211	B2	19970130		
EP 608320	A1	19940803	EP 1992-921755	19921013 <--
EP 608320	B1	19980128		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE				
HU 74560	A2	19970128	HU 1994-1107	19921013 <--
AT 162725	T	19980215	AT 1992-921755	19921013 <--
ES 2114569	T3	19980601	ES 1992-921755	19921013 <--
CN 1072863	A	19930609	CN 1992-112390	19921016 <--
IN 178157	A1	19970308	IN 1992-DE1011	19921105 <--
IN 181010	A1	19980411	IN 1992-DE1013	19921105 <--
NO 9401319	A	19940616	NO 1994-1319	19940413 <--
FI 9401771	A	19940415	FI 1994-1771	19940415 <--
US 5756118	A	19980526	US 1995-462258	19950605 <--
US 5756119	A	19980526	US 1995-462376	19950605 <--
US 5773023	A	19980630	US 1995-462710	19950605 <--
US 5780049	A	19980714	US 1995-464991	19950605 <--
US 5776485	A	19980707	US 1995-469701	19950606 <--
US 5874095	A	19990223	US 1998-49367	19980327

PRIORITY APPLN. INFO.:
US 1991-778424 A 19911016
US 1992-957752 B1 19921002
WO 1992-US8741 A 19921013
US 1993-111032 B1 19930824
US 1994-228167 B1 19940415
US 1995-390902 B3 19950216
US 1995-462710 B3 19950605

PI WO 9307902 A1 19930429

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9307902	A1	19930429	WO 1992-US8741	19921013 <--
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO,				

PL, RO, RU, SD
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG

AU 9228064	A	19930521	AU 1992-28064	19921013	<--
AU 675211	B2	19970130			
EP 608320	A1	19940803	EP 1992-921755	19921013	<--
EP 608320	B1	19980128			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE					
HU 74560	A2	19970128	HU 1994-1107	19921013	<--
AT 162725	T	19980215	AT 1992-921755	19921013	<--
ES 2114569	T3	19980601	ES 1992-921755	19921013	<--
CN 1072863	A	19930609	CN 1992-112390	19921016	<--
IN 178157	A1	19970308	IN 1992-DE1011	19921105	<--
IN 181010	A1	19980411	IN 1992-DE1013	19921105	<--
NO 9401319	A	19940616	NO 1994-1319	19940413	<--
FI 9401771	A	19940415	FI 1994-1771	19940415	<--
US 5756118	A	19980526	US 1995-462258	19950605	<--
US 5756119	A	19980526	US 1995-462376	19950605	<--
US 5773023	A	19980630	US 1995-462710	19950605	<--
US 5780049	A	19980714	US 1995-464991	19950605	<--
US 5776485	A	19980707	US 1995-469701	19950606	<--
US 5874095	A	19990223	US 1998-49367	19980327	

IT Anesthetics
Anti-infective agents
Antiarrhythmics
Antidepressants
Antiemetics
Antihistaminics
Antihypertensives
Antimalarials
Antitussives
Appetite depressants
Cardiotonics
Cholinergic agonists
Diuretics
Hypnotics and Sedatives
Inflammation inhibitors
Muscle relaxants
Neoplasm inhibitors
Nervous system stimulants
Sunscreens
Tranquilizers and Neuroleptics
Ulcer inhibitors
Vasoconstrictors
Vasodilators
Wound healing promoters
(topical compns. containing polyacrylamide and)

IT 55-56-1, Chlorhexidine 57-62-5, Chlortetracycline 57-92-1, Streptomycin, biological studies 59-01-8, Kanamycin 74-55-5, Ethambutol 79-57-2, Oxytetracycline 100-33-4, Pentamidine 100-97-0, biological studies 154-21-2 443-48-1, Metronidazole 564-25-0 768-94-5, Tricyclo[3.3.1.13,7]decan-1-amine 914-00-1, Methacycline 1403-66-3, Gentamicin 1404-04-2, Neomycin 3380-34-5, Triclosan 7542-37-2, Paromomycin 10118-90-8, Minocycline 11003-38-6, Capreomycin 22916-47-8, Miconazole 32986-56-4, Tobramycin 37517-28-5, Amikacin 56391-56-1, Netilmicin 70458-96-7, Norfloxacin 85721-33-1, Ciprofloxacin
RL: BIOL (Biological study)
(antimicrobial topical compns. containing polyacrylamide and)

L18 ANSWER 14 OF 14 USPATFULL on STN

ACCESSION NUMBER:	93:26884 USPATFULL
TITLE:	Oral osmotic device
INVENTOR(S):	Edgren, David E., El Granada, CA, United States Bhatti, Gurdish K., Fremont, CA, United States
PATENT ASSIGNEE(S):	ALZA Corporation, Palo Alto, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 5200194		19930406	<--
APPLICATION INFO.:	US 1991-809741		19911218	(7)
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	Granted			
PRIMARY EXAMINER:	Page, Thurman K.			
ASSISTANT EXAMINER:	Horne, Leon R.			
LEGAL REPRESENTATIVE:	Duvall, Jean M., Miller, D. Byron, Stone, Steven F.			
NUMBER OF CLAIMS:	19			
EXEMPLARY CLAIM:	1			
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 1 Drawing Page(s)			
LINE COUNT:	880			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . (LISTERINE sold by Warner-Lambert Co. of Morris Plains, N.J.); benzophenathradine (VIADENT sold by Vipont Pharmaceutical, Inc. of Fort Collins, Colo.); triclosan and zinc citrate; stannous fluoride; and cetylpyridinium chloride (CEPACOL sold by Marion Merrell Dow of Cincinnati, Ohio and SCOPE sold. . .

DETD . . . sedatives, psychic energizers, tranquilizers, anticonvulsants, muscle relaxants, antiparkinson agents, analgesics, anti-inflammatory drugs, local anesthetics, muscle contractants, anti-plaque agents, anti-microbials, anti-fungals, anti-malarials, hormonal agents, contraceptives, sympathomimetics, diuretics, anti-parasitics, neoplastics, hypoglycemics, ophthalmics, electrolytes, diagnostic agents, and cardiovascular drugs.

DETD . . . alkaloids such as sanguinarine and sanguinarine chloride, metal salts such as zinc citrate, non-charged phenolic agents such as thymol and triclosan, enzyme systems such as mutanases, amylogycosidase and glucose-oxidase, sugar substitutes such as xylitol and mannitol, fluorides such as stannous fluoride. . .

CLM What is claimed is:
. . . benzalkonium chloride, aminacridine hydrochloride, mepacrine hydrochloride, hydrogen peroxide, potassium peroxidiphosphate, proguanil hydrochloride, dibromopropamidine diisothionate, hexidine, alexidine, octenidine, zinc citrate, thymol, triclosan, mutanases, amylogycosidase, glucose-oxidase, xylitol, mannitol, stannous fluoride, sodium fluoride, decapinol, sodium polyvinylphosphonic acid, perfluoroalkyl surfactants and cetyldimethylbenzyl ammonium chloride.

CLM What is claimed is:
. . . benzalkonium chloride, aminacridine hydrochloride, mepacrine hydrochloride, hydrogen peroxide, potassium peroxidiphosphate, proguanil hydrochloride, dibromopropamidine diisothionate, hexidine, alexidine, octenidine, zinc citrate, thymol, triclosan, mutanases, amylogycosidase, glucose-oxidase, xylitol, mannitol, stannous fluoride, sodium fluoride, decapinol, sodium polyvinylphosphonic acid, perfluoroalkyl surfactants and cetyldimethylbenzyl ammonium chloride.

IT 54-21-7, Sodium salicylate 56-95-1, Chlorhexidine diacetate 64-17-5, Ethanol, biological studies 69-05-6, Mepacrine hydrochloride 69-65-8,

Mannitol 87-99-0, Xylitol 89-83-8, Thymol 122-18-9, Cetyldimethylbenzylammonium chloride 123-03-5, Cetylpyridinium chloride 134-50-9 522-51-0, Dequalinium chloride 532-32-1, Sodium benzoate 546-46-3, Zinc citrate 614-87-9 637-32-1, Proguanil hydrochloride 1330-43-4, Boron sodium oxide (B4Na2O7) 2447-54-3, Sanguinarine 3380-34-5, Triclosan 3697-42-5 5578-73-4, Sanguinarine chloride 7681-49-4, Sodium fluoride, biological studies 7722-84-1, Hydrogen peroxide, biological studies 7783-47-3, Stannous fluoride 9001-37-0, Glucose oxidase 9032-08-0 9075-84-7, Mutanase 15593-49-4 18472-51-0, Hexidine 22573-93-9, Alexidine 60406-21-5 62571-86-2 71251-02-0, Octenidine 79874-76-3, Decapinol
(therapeutic oral osmotic device containing)